

# SCIENCE

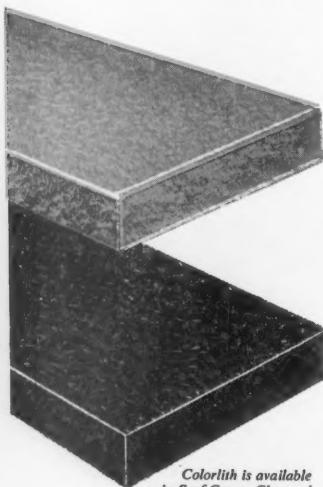
15 August 1958

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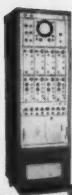


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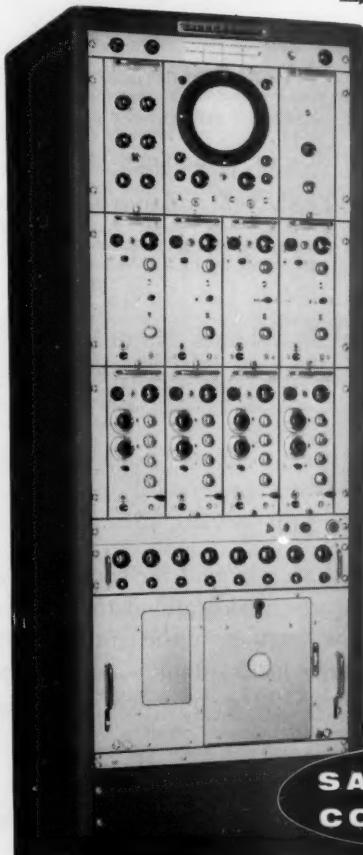
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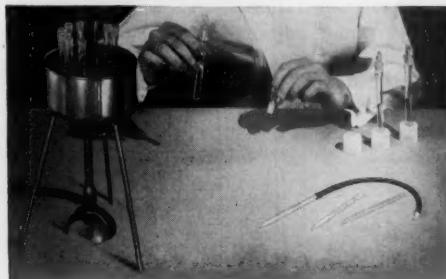
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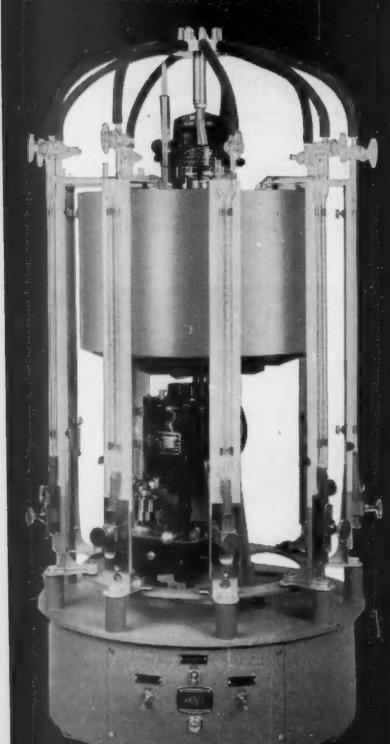
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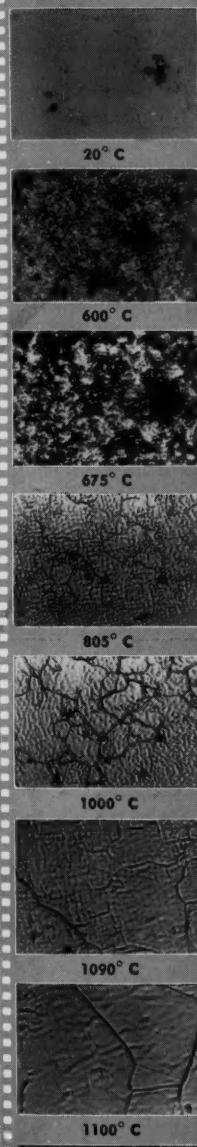
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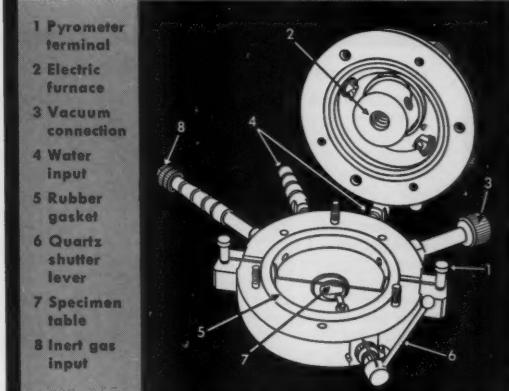
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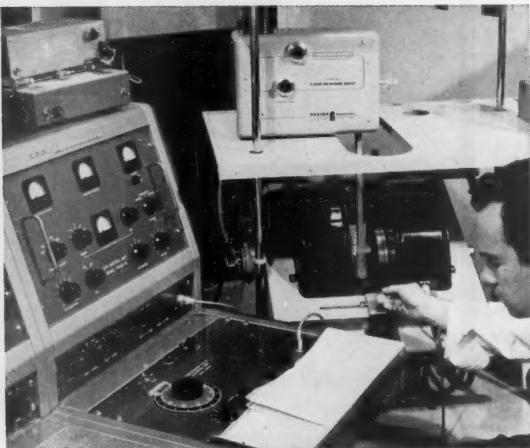


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FIGURE 1 Electron Irradiated L-Glutamic Acid

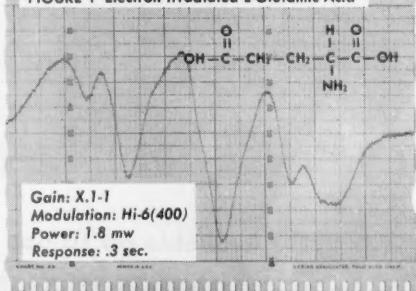
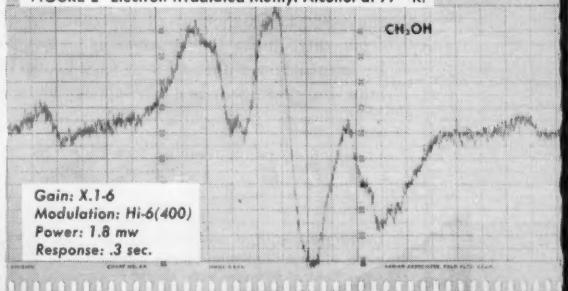


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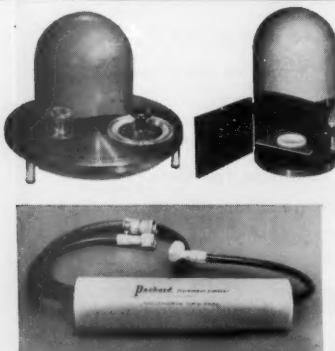
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*Science* hesitated because there are disadvantages as well as advantages to the bingo game. The advantage to the reader is that it gives him a quick and easy method to indicate the things about which he would like to learn more. He can do it while he is reading, and does not need to remember sometime later to dictate a letter, or to write one himself. If there are several items in the same issue that interest him, one coupon takes care of inquiries about all. From the advertiser's standpoint there is also an advantage: he gets a quick and easy index of the amount of interest in the product he is advertising.

The principal objection is on the advertiser's side rather than the reader's, but some advertisers fail to recognize it. The bingo card invites a more casual, less sincerely interested inquiry than is received if an individual letter must be written. Advertisers are always interested in knowing the nature as well as the size of the circulation of a magazine in which they are contemplating placing an advertisement. Yet some of these same advertisers are content to measure the effectiveness of an ad by the total number of inquiries, regardless of their nature or quality. Perhaps, having already decided to place an ad in a particular magazine, it is advantageous to secure as many inquiries as possible; as a minimum, the list of prospects is increased. But some advertisers are more discriminating. Those who keep good count of all types of inquiries—individual letters as well as coupons—and who appraise their ads in terms of actual sales frequently report that, while *Science* produces a comparatively small number of inquiries, the ones that are received are of high quality and result in substantial sales volume. The less discriminating method of simply counting the total number of inquiries gives less credit to *Science* and less help to the advertiser.

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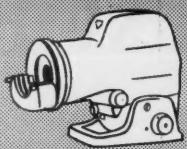
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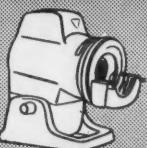


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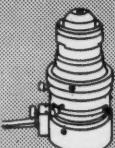
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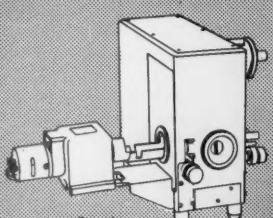
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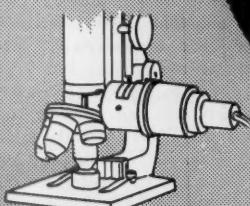
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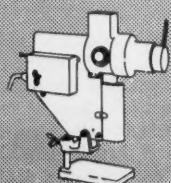
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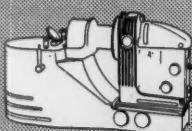
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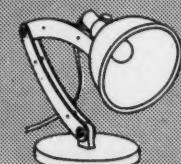
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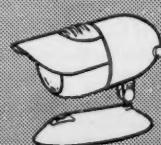
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CURRENT PROBLEMS IN RESEARCH

## Stabilized Pinch and Controlled Fusion Power

Study of the pinch effect has caused ups and downs in the hopes for building a thermonuclear reactor.

S. A. Colgate and H. P. Furth

Controlled fusion power (1) is an exciting possibility, because the proposed fuels, deuterium and tritium, are obtainable in almost unlimited supply from the ocean. Unfortunately, the operation of a fusion reactor is unlike that of a fission reactor in that the reaction cannot be initiated simply by assembling the fuel elements. Only by preheating the fuel to from  $10^8$  to  $10^9$  degrees Kelvin and maintaining such temperatures at least for an appreciable fraction of a second can fusion power be generated in a controllable manner. The stabilized pinch is one of the several "magnetic bottles" that have been proposed to solve the heating and containment problem. Large-scale pinch research is being conducted by the Atomic Energy Commission at the Berkeley, Livermore, and Los Alamos sites of the University of California.

When a strong current is passed through a tube filled with ionized gas, or plasma, a contraction of the plasma column results (Fig. 1). This so-called "pinch effect," first described by Willard Bennett (2) in 1934, has turned out to have many useful features. The large current in the pinch column serves to heat the plasma, as does the compression associated with the pinching. A toroidal stabilized pinch (Fig. 2) is an example of a perfectly closed magnetic bottle. The magnetic field and plasma distribution in this bottle is nearly op-

timal, from the point of view of reactor economics. Such considerations have kindled high hopes for the pinch as a successful fusion machine.

In what follows it will perhaps become clear that the achievement of a power-producing pinch device is not really very close at hand. This result is not disappointing, since present experiments are not meant to fall into the realm of reactor technology but into that of basic plasma research. The substantial scale on which pinch research is conducted the world over reflects not so much the imminence or inevitability of success as the high potential value of knowledge about thermonuclear plasmas. The same comment applies in the case of the various other magnetic bottles that are being studied intensively at present (3). In each instance a plausible design for an ultimate power-producer serves to orient research, but the immediate objective is to learn about some feature of plasma physics. What composite or entirely novel fusion machine will emerge from this basic research effort remains to be seen.

### The Unstable Pinch

In the course of early experiments with the pinch effect (4) it was found that the simple pinch configuration (Fig. 1) is violently unstable. The plasma particles are indeed kept tightly in the magnetic bottle while it lasts, but the bottle

itself soon falls apart. In the experiments, destruction occurred after a few microseconds—an interval far short of useful thermonuclear reaction times. The predominant instability was found to be the "sausage" mode predicted by the theory of Kruskal and Schwarzschild (5) (Fig. 3a). The transient plasma temperatures which the pinching process would create before breakup of the configuration were also estimated on a theoretical basis (6). High-powered experiments to investigate the predicted plasma heating effect were soon under way.

During 1955, pinches at Berkeley and later at Los Alamos were found to emit large quantities of neutrons. It was thought reasonable to conclude that a thermonuclear plasma of some millions of degrees had been achieved. Experiments on the timing, symmetry, and localization of the neutrons (7) seemed to confirm the thermonuclear hypothesis. We noted, however, that neutrons could be produced under conditions where the theory clearly predicted nonthermonuclear plasma temperatures. Thanks to some lingering doubts on this point, a nuclear track plate experiment was done in Berkeley in late 1955, which showed that the neutrons were indeed produced by a "spurious" effect (8).

It may be helpful here to explain just why the distinction between thermonuclear and nonthermonuclear neutrons is of consequence in fusion research. The production of fusion reactions as such is not very difficult and can be accomplished by any number of particle accelerators the world over. A beam of deuterons is accelerated, say to 100 kev energy, and allowed to impinge on a cold deuterium target. Some of the incident deuterons will fuse with target deuterons, releasing energetic neutrons. The difficulty with this approach is that more energy is always degraded into heat than is regenerated by the fusion reactions. On such a basis it is impossible to produce power. In a power-producing reactor the deuterons must be able to collide with each other many times without degradation of energy (1). This requirement defines a *thermalized* assembly of reacting particles—a so-called thermonuclear plasma.

A thermal deuterium plasma does not

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produce measurable neutron yields below a few million degrees temperature. Just above this threshold the increase of the yield with increasing temperature is extremely steep. If a given neutron-emitting plasma is also a thermal plasma, the plasma temperature can be calculated with high precision from the neutron yield. Such a "neutron thermometer" gives some measure of the degree of progress toward practical thermonuclear conditions. If a neutron-emitting plasma is *not* thermalized—that is (if the neutrons are caused by a small population of energetic deuterons reacting with an otherwise cold plasma—then the yield is obviously not indicative of high plasma temperature or of progress toward the conditions of a fusion reactor. In that case one speaks of spurious or nonthermonuclear neutron yields.

The nuclear track plate experiments which were done in 1955 on the unstable pinch showed that the neutrons were generated by a 10<sup>-3</sup>-percent population of deuterons moving with 40 kev mean energy in the direction of the pinch current, rather than by a uniformly hot plasma of 10 million degrees (or 1 kev) temperature. The most plausible explanation (8) seemed to be that the energetic deuterons were accelerated by intense local electric fields set up at the unstable constrictions of the pinch column (Fig. 3a). How high a plasma temperature has actually been reached in unstable pinch experiments is not known. Part of the difficulty is that the spurious neutron yield masks any true yield that may be coming from the thermalized part of the plasma. In this way the large neutron emissions, which were welcomed with enthusiasm at first, have become a nuisance to the experimenter.

Soon after the Berkeley experiment,

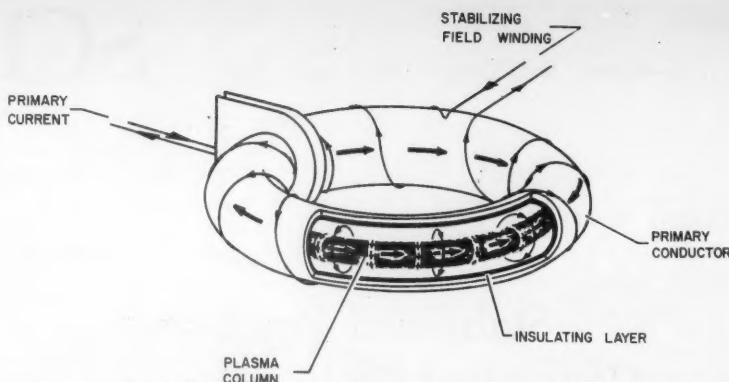


Fig. 2. A toroidal stabilized pinch. The primary current on the shell induces a longitudinal opposing current in the plasma, which pinches the discharge. During pinch formation, the longitudinal stabilizing field is trapped in the plasma, and the current in the stabilizing winding comes to a stop. At the same time, an azimuthal surface current appears on the plasma.

I. V. Kurchatov created a sensation at Harwell (9) by reporting on neutron emission from unstable pinch devices in the U.S.S.R. It turned out that the Russian pinch program had also undergone a cycle of high expectations and sobering afterthoughts some years before. We were particularly impressed by the good judgment of the Russian scientists in doubting that a thermonuclear plasma had been achieved even though they did not have available the definitely nonthermonuclear evidence of the nuclear track plate experiment.

### Stabilization of the Pinch

Early in 1956 the philosophy of the United States pinch program underwent an important development. Heretofore the instability of the pinch effect had been regarded as a necessary evil. The principal aim had been to achieve and study thermonuclear plasma conditions during the very short time interval between pinch formation and breakup. It was now recognized that the pinch could be made stable.

The retarding influence of a longitudinal magnetic field on pinch instabilities had been calculated in 1953 by Kruskal and Tuck (10). During 1954, the importance of trapping a longitudinal magnetic field *inside* the pinch column was emphasized by Morton Levine, in an unclassified Tufts College report (11). It was also shown by Levine (12) and others that a close-fitting cylindrical return-conductor on the pinch tube would create a stabilizing effect. A rigorous mathematical theory of pinch stability was produced by Marshall Rosenbluth (13) in the spring of 1956.

When a longitudinal magnetic field is trapped inside the pinch column, it is fairly obvious that the sausage instability mode is inhibited (Fig. 3b). In this case the most violent remaining instability is the "kink" mode of Fig. 3c. Rosenbluth proved that by the joint influence of the trapped longitudinal magnetic field and a close-fitting return conductor, the kink instability could be suppressed (Fig. 3d), as could all the other less violent modes. The detailed conditions under which this stable regime is achieved are quite restrictive. No pinch is stable if the radial compression is greater than 5:1 or if the plasma pressure exceeds the longitudinal magnetic field pressure. In addition, it is essential that there be little or no longitudinal magnetic field in the region outside the pinch column.

The predictions of the Rosenbluth stability theory have been investigated experimentally at some length (14). The procedure was to wrap a solenoid around a linear pinch tube containing neutral gas and to pass a slow-rising current through this winding. A longitudinal magnetic field then appeared in the tube. At this point we would ionize the gas and pass a fast-rising pinch current through it. A plasma column was then formed as usual, with the longitudinal magnetic field trapped inside. Trapping of magnetic field in plasma occurs, of course, by virtue of the electrical conductivity of the plasma. A more familiar form of the same phenomenon is the so-called "skin effect." A high-frequency current can flow along a conductor only in a shallow surface layer, because the magnetic field of the current cannot pass readily into the interior. In the case of stabilized pinch the situation is reversed: the magnetic field is prevented from

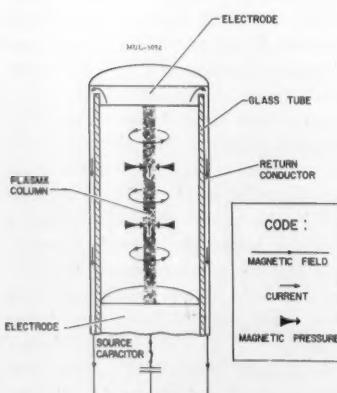


Fig. 1. The simple, unstable pinch.

passing rapidly out of a conductor—namely, the pinch. As the pinch is formed, a layer of azimuthal skin current begins to flow around the plasma column. One can think of the azimuthal current layer as the field-generating solenoid that accompanies the entrapped longitudinal magnetic field.

As the pinch column contracts, the longitudinal magnetic field grows in intensity, so that a magnetic back-pressure develops. The pinch compression proceeds to a point where the pressure of the trapped longitudinal field and plasma precisely equals the pressure of the azimuthal field outside the pinch column. In the experiments, the degree of compression was controlled by altering the magnitude of the initial longitudinal field. When the longitudinal field was made small or null, the resultant pinch proceeded to a high compression and was almost immediately unstable. When the conditions of the Rosenbluth theory were met, we observed a transient interval of stability, lasting some ten times longer than the life-time of the discharge when unstabilized.

The importance of avoiding longitudinal magnetic field outside the pinch column was also demonstrated unequivocally by the experiments. When a pinch was formed, all the longitudinal field passing through the gas would be trapped inside. Additional magnetic field was prevented from entering the discharge tube during the pinch time because of the solid conductor shell surrounding the tube. However, there remained a small amount of longitudinal magnetic flux in the cross section of the glass itself. The passage of this flux into the region between the pinch column and the tube wall had a critical influence on the stability of the discharge. We were able to show that under otherwise identical conditions the pinch would be stable or unstable depending on whether the glass wall of the discharge tube was thin or thick.

This disruptive influence of magnetic field outside the pinch column manifested itself in still another interesting way. By means of a small search-coil, we observed that in a thin-walled discharge tube the magnetic field near the

tube wall would drop to very low values during pinch compression. This was exactly as desired. For stable compressions, the signal remained near zero for a while and, if the pinch current was maintained sufficiently long, would then actually swing negative (Fig. 4a). Kerr cell pictures taken at the time of the anomalous negative signal showed that the pinch had wrapped itself into a helix (Fig. 4b). The explanation was not difficult to find. Because of the poor electrical conductivity of the plasma, neither the longitudinal magnetic field nor the plasma itself could be expected to remain perfectly trapped in the space of the original pinch column. A diffuse layer of mixed longitudinal and azimuthal magnetic field was soon formed at the surface of the discharge. As the layer broadened, the configuration acquired unstable tendencies, precisely like those of an undiffused pinch with some longitudinal field outside it. Eventually the kink instability developed. As predicted by Rosenbluth's theory, the kinks aligned themselves in such a way as to form a helix. This helix, acting as

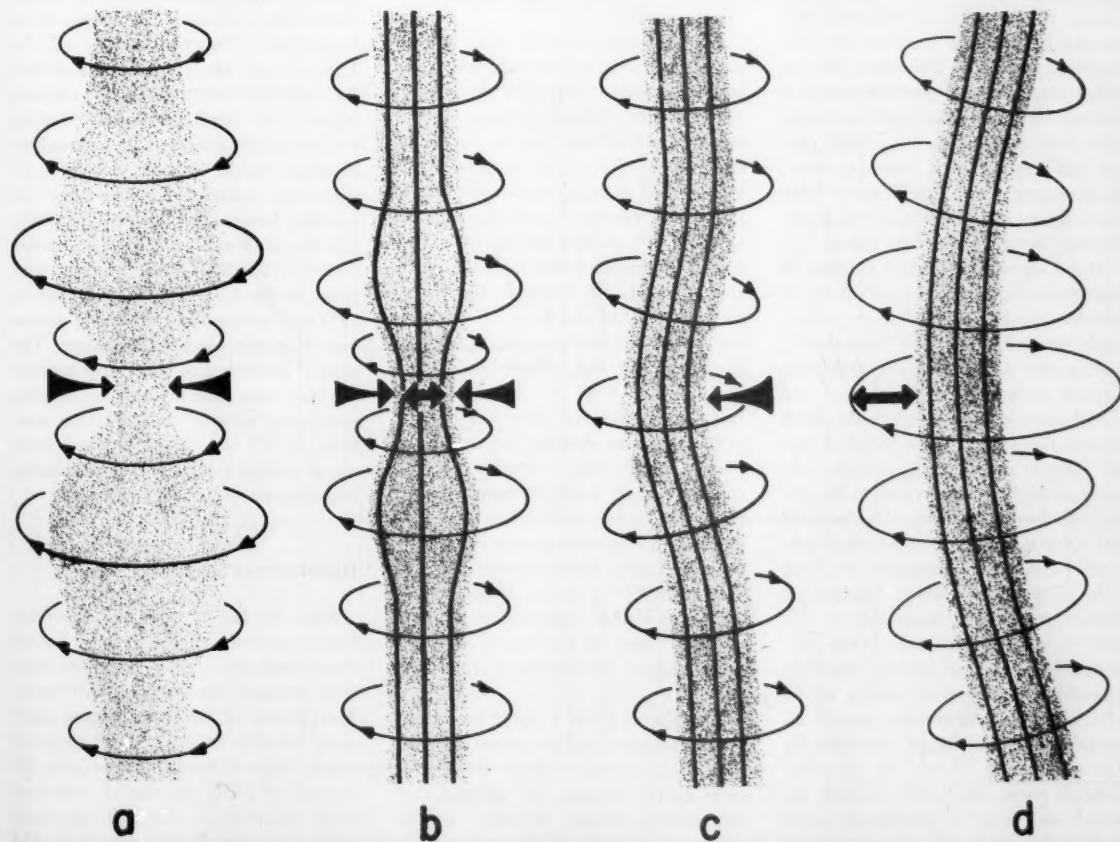


Fig. 3. (a) The sausage mode of the simple pinch; (b) the stabilization of the sausage mode by an included longitudinal field; (c) the kink mode; (d) the stabilization of the kink mode by a conducting shell. The heavy arrows indicate magnetic pressures.

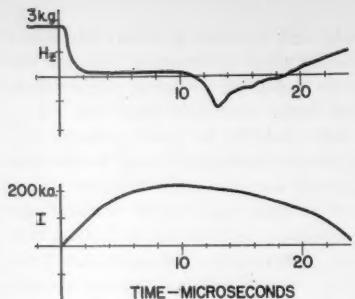
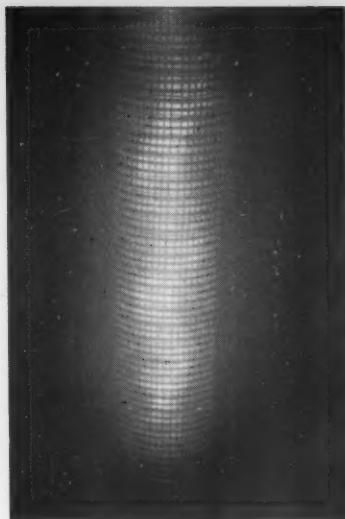


Fig. 4. (a) (Above) Variation of the longitudinal magnetic field at the tube wall of a stabilized pinch. The sudden negative swing of the signal indicates the onset of a helical instability mode. (b) (Right) A Kerr cell picture of the helical instability.

a kind of solenoid, produced a negative longitudinal magnetic field at the tube wall.

The maximum stable time of the pinch was now seen to depend on the rapidity with which the original pinch configuration became diffuse (Fig. 5). As is well known, the duration of diffusion phenomena in a system increases with the square of the linear dimension. For instance, the head of a pin will cool in a millisecond when immersed in water, while heat diffusion out of a large cannon ball may require a minute or more. In the same way, a sufficiently large pinch device can obviously be kept stable long enough to produce power.

At the outset of the pinch program it was recognized that the life-time of an *unstable* pinch could be made appreciable simply by building a large device. In this case the instability growth time depends essentially on the transit time of hydromagnetic waves across the pinch column. Consequently the period of useful plasma containment increases directly as the linear dimension of the system. Early calculations demonstrated that a reactor of the unstable pinch type would have to be of enormous size. Each cycle of operation would liberate an amount of energy comparable to the yield of a hydrogen bomb. When contrasted with such an infernal machine, a moderately large-scale version of the stabilized pinch experiment seemed almost reasonable, though economically still unattractive. From the economic point of view, the really hopeful approach was to try to prolong the stable time of the pinch, not by increasing its size very much but, rather, by reducing



the diffusion constant of the plasma. The logic of this procedure can be made appealing by recourse to the heat diffusion analogy: If one wishes to keep cold ice cream available for a certain length of time, it is clearly more practical to find a thermos bottle than to fill up the bathtub.

The diffusion constant that governs the deterioration of the stabilized pinch is the electrical resistivity of the plasma. If the plasma resistivity is large, the stabilizing field diffuses rapidly out of its confinement, just as the magnetic field of a pulsed solenoid decays rapidly if the circuit resistance is large. The resistivity of a plasma can be calculated from the number-density and the mean free path of the electrons that carry the current. On the basis of electron-ion scattering cross sections it is easy to show (15) that plasma conductivity improves with the  $3/2$  power of the temperature and does not depend very much on density. A deuterium plasma of 10 million degrees has the conductivity of standard copper. Since the conductivities observed in the stabilized pinch experiments were more than a hundred times lower, corresponding to about  $300,000^{\circ}\text{C}$ , it was reasonable to anticipate a great improvement in pinch diffusion times as soon as 10- to 100-million-degree temperatures could be reached.

In diffusing from a stable to an unstable configuration, the magnetic fields of the pinch lose a certain fraction of their energy content. We showed that the missing energy, delivered to the plasma in the form of ohmic heating, is always of just the right magnitude to

raise the plasma to a useful temperature. Here it is assumed that the heating rate is sufficiently high to overcome loss mechanisms such as bremsstrahlung. A detailed calculation of a pinch heating and reaction cycle based on the diffusion principle has been made by Rosenbluth (16).

If high plasma temperatures are to be maintained in the pinch during long reaction times, it is of course essential to eliminate heat conduction along the longitudinal field lines, into the electrodes. For this purpose one passes from linear to toroidal geometry (Fig. 2). The toroidal pinch tube is a kind of pulse transformer in which the conductor shell is the primary and a pinched ring of plasma constitutes the secondary. Separation of the primary and secondary is achieved by means of a toroidal insulator tube or lining. An iron core is often used to improve the coupling between the primary current and the pinch current. The physics of the toroidal pinch is essentially that of a linear pinch having infinite length.

The development of the stabilized pinch reactor scheme has been the major original contribution of United States pinch research to fusion reactor technology. The publications of the U.S.S.R. have dealt mostly with powerful unstable discharges (17). Several papers (18) have appeared describing pinches partly stabilized by longitudinal magnetic fields, but the possibility of achieving complete stabilization by avoiding longitudinal magnetic field outside the pinch appears to have been overlooked (19). The pinch research program of the United Kingdom prior to 1957 was oriented toward taking advantage of partly unstable discharges. The plan of attack was to build large toroidal discharge tubes and to allow the unstable pinch to "wriggle" within these confines. In this way, powerful shock heating as well as a limited form of plasma containment could be anticipated.

#### High-Powered Stabilized Pinches

Since the fall of 1956, the controlled fusion research efforts of the United States and the United Kingdom have been brought into close collaboration. This joining of forces has proved especially valuable in the field of pinch research, which is the British specialty. By the end of 1956, the size of American pinch installations was still extremely modest. Almost all the experiments had been done with tubes of from 2 to 4

inches in diameter, powered by capacitor banks in the  $10^4$ -joule range. The British were already using tubes a foot in diameter and were planning Zeta, a toroidal pinch device with a 3-foot bore, powered by a 1-million-joule capacitor bank. Among the fruitful techniques developed at Harwell were the use of all-metal pinch tubes and the operation of pinch discharges in very low densities of deuterium.

The American contribution to the joint research effort was a dogmatic insistence on complete pinch stabilization. The British scientists had already done some thinking along this line (20) and were readily converted. Zeta, which originally had been planned as the most advanced of the "wriggling" pinches, underwent some rewiring and turned out to be the most advanced of the stabilized pinches. Experimentation with Zeta began in the late summer of 1957 and immediately yielded important results. In the small pinch devices, the time of stable operation had been only about 10 microseconds, or about ten times longer than a typical instability growth time. Zeta, being ten times larger in diameter, remained stable for

a millisecond, or a hundred times longer than a typical instability growth time. In this way, the gross stability of the configuration was far more clearly demonstrated than in the smaller experiments. Much to our disappointment, the electrical conductivity in Zeta turned out to be rather worse than it had been in the little pinch devices. A temporary distraction from this result was afforded by the observation of neutrons coming from the discharge (21).

The theoretical maximum plasma temperature in Zeta was about 20 million degrees. It was therefore conceivable that the observed neutrons might be coming from a 5-million-degree thermonuclear plasma. Measurements on the Doppler broadening of impurity spectra supported this possibility. Certain particulars in the timing and magnitude of the neutron signal seemed odd, but we were all sufficiently impressed by the performance of Zeta to entertain the thermonuclear hypothesis.

Around the Christmas season of 1957, Sceptre, a toroidal stabilized pinch of 12-inch bore, began to yield neutrons (22), as did Perhapsatron S-3 in the 2-inch size (23) and Gamma Pinch

(24) at 4 inches. Even more surprising, Columbus S-2, a linear stabilized pinch (25) was emitting neutrons, though such devices had not been expected to reach thermonuclear temperature, because of heat losses to the electrodes. In the Los Alamos experiments (23, 25), the magnetic field distributions of the pinches were studied and were shown to imply plasma pressures indicative of thermonuclear temperature. In all the experiments the electrical conductivity proved to be about the same—namely, far below what the classical theory would predict at the 3- to 6-million-degree temperatures required by a thermonuclear explanation of the neutrons.

The conductivity results were taken by us as indicative of rather poor plasma conditions, or at least of poorly understood conditions, and as a result a spirit of cautious skepticism developed at Livermore (26). The early observations made on Zeta had been somewhat confidence-inspiring, but the wealth of neutronics data which was now becoming available from the smaller machines showed that neutrons were often produced under extremely unsanitary conditions. We were soon led to conclude

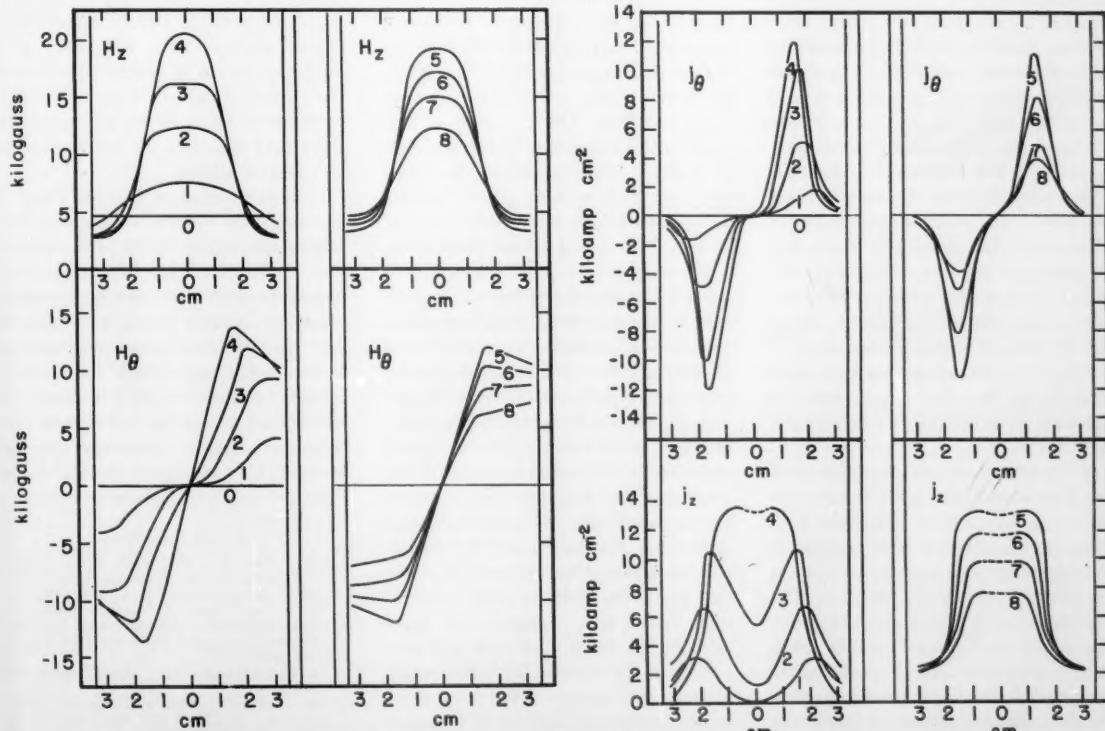


Fig. 5. Magnetic field and current distributions in a linear stabilized pinch, as measured with search-coils. The curve labels refer to microseconds after pinch initiation. The longitudinal and azimuthal magnetic fields are shown interdiffusing, but the current cycle is kept short enough to avoid instability.

that the stabilized pinch was subject to a spurious neutron production mechanism, just as the unstable pinch had been. All the neutron-emitting machines had certain important parameters in common, such as the magnitude of the pinch current, the number of plasma particles per unit length of the discharge, and the proportion of the pinch cycle time to the square of the tube radius. The neutronics data from all the machines showed a remarkable consistency in their dependence on voltage, pinch compression ratio, plasma density, and impurity admixture. Accordingly, if the thermonuclear claim could be made for any of the machines, it had to be made for all of them. In view of the accumulating discrepancies, we thought it more likely that all the machines were equally subject to some nonthermonuclear mechanism of neutron production.

The Doppler-broadened spectra obtained with Zeta could be explained in terms of local plasma turbulence just as readily as in terms of high temperature. The large apparent plasma pressures found at Los Alamos by means of magnetic probe analyses were interpretable as pressures of turbulent motion. Conversely, it was argued that the low temperatures estimated on the basis of the electrical conductivity were unrealistic, because resistivity might be enhanced by various plasma oscillations. Arguments based on conservation of energy seemed to indicate very high temperatures, but it was shown on Gamma Pinch that a large anomalous heat-transfer effect was taking place between the discharge and the tube walls. Still another debatable estimate of temperature was afforded by the degree of stripping of impurity ions, such as oxygen. The presence of three-, four-, and five-times-stripped oxygen and the absence of the six-times-stripped ion in Zeta were interpreted by various methods as implying temperatures of anywhere from 200,000 to 5 million degrees.

Recently the edge of the controversy has been dulled somewhat by the discovery on Zeta that the observed neutrons are caused by a small population of high-energy deuterons accelerated in the direction of the current (27). The experiment, done with a cloud chamber, was very similar to the nuclear track plate experiment, which had earlier diagnosed the neutrons from the unstable pinch as nonthermonuclear. Shortly after the Zeta results were known, the same experiment was done at Los Alamos on Perhapsatron S-4, a 4-inch to-

roidal pinch (28). The Los Alamos findings have proved identical with those obtained on Zeta. The mechanism of deuteron acceleration is still undetermined. There is some evidence both for and against a simple "running away" of deuterons in the applied electric field of the discharge.

The disillusioning experience with neutrons from the stabilized pinch, coming on top of the similar experience with neutrons from the unstable pinch, seems to convey a lesson. Heretofore the interpretation of neutronics results has been approached on the basis of a pre-conceived model, the thermonuclear plasma. On measuring a given neutron yield, experimenters have quoted a corresponding temperature. The logic of this procedure is extremely precarious, especially in the case of small neutron yields. Most of the fusion reactions of a low-temperature thermonuclear plasma are produced by particles far out in the high-energy tail of the Maxwellian distribution. Even on observing a neutron yield produced by an isotropic deuteron population that might perhaps constitute the high-energy component of a thermonuclear plasma, one cannot logically demonstrate the presence of the Maxwellian distribution from the presence of its tail. Judging from present indications, the pure Maxwellian energy distribution may turn out to be an experimental rarity, rather than the most likely possibility. One is forced to conclude that temperature estimates should be based, not on neutronics, but on a thorough study of bulk plasma properties, coupled with a theoretical understanding of the observed phenomena. Unfortunately, scientific knowledge of this kind is only slowly becoming available in the case of the stabilized pinch.

Electrical conductivity measurements on Zeta and the other recent devices all point to temperatures of about 100,000 degrees, an even lower figure than characterized the old linear stabilized pinch experiments. This result carries with it a suggestion that conditions are worse, at least in some respects, in the high-powered pinch experiments of 1958 than in the low-powered experiments of 1956. One possibility is that plasma temperatures are actually lower in the high-powered machines. A second and perhaps more likely possibility is that actual plasma temperatures differ from those computed on the basis of the classical theory of conductivity. This alternative is supported by recent analyses of impurity stripping in Zeta, which indicate

temperatures between 300,000 and 500,000 degrees.

While the so-called "stabilized" pinch has been shown to be highly stable in a gross sort of way, evidence is now accumulating that small-scale turbulence exists within the gross configuration. Under these circumstances, it is not surprising that the electrical conductivity of the discharge is low and becomes lower at higher power levels. If the mean free path of the current-carrying electrons is being kept short not by electron-ion collisions but by electron interactions with hydromagnetic and electrostatic plasma waves, then one may anticipate a consistent shortening of the mean free path as more energy is made available for the excitation of the waves. If this theory proves correct, then pinch research is on the threshold of an important plasma-physical discovery. At the same time, the existence of an enhanced resistivity effect at high power levels would raise doubts about the stabilized pinch as a long-time, high-temperature plasma container. In this context it should be recalled that the function of a magnetic bottle is just precisely the long-time containment of hot plasma, not the achievement of fusion reactions, which can be duplicated by a simple accelerator. Even if 100-million-degree plasmas were eventually produced by means of pinch experiments, the failure to achieve long-time stable containment in a device of reasonable size would eliminate the pinch as a fusion reactor scheme.

Current research on Gamma Pinch is yielding some suggestive results on the role of runaway electrons in the excitation of plasma waves (14), and we are looking forward with interest to experiments on a more powerful version of Zeta that will soon go into operation at Harwell. The opportunity for a broad review of world-wide pinch research will be afforded by the Second United Nations International Conference on the Peaceful Uses of Atomic Energy, to be held in Geneva in September (29).

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## Radiation and the Sex Ratio in Man

Sex ratio among children of survivors of atomic bombings suggests induced sex-linked lethal mutations.

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In species with an XX-XY type of chromosomal sex determination, such as man, the distribution to the offspring of radiation-induced, sex-linked mutations will differ according to the sex of the irradiated parent. Furthermore, in the human species the nonhomologous nature of the X- and Y-chromosomes, coupled with the genetic inertness of the Y, permits the more frequent manifestation of sex-linked recessive genes in the heterogametic sex—namely, the male. This difference in manifestation and distribution of sex-linked genes would lead us to expect a significant change in the sex ratio if human populations were sufficiently exposed to mutagenic factors such as x-rays, or the fallout from weapon testing. Specifically, if fathers alone were exposed, an increase in the frequency of male births would be expected because

sex-linked lethal mutants induced by the exposure would be transmitted only to the exposed fathers' daughters. If mothers alone were exposed, a decrease in the frequency of male births would be expected because sex-linked recessive mutants would more frequently find expression in the sons rather than in the daughters of the exposed females. If both parents were exposed, and if the effects of parental exposure were additive although not necessarily equal, we would expect a decrease in the frequency of male births; the change, however, would not be expected to be as pronounced as when mothers alone were exposed.

### Assumptions

Several assumptions are implicit in postulating the changes just mentioned, and it seems important to state explicitly, at the outset, these assumptions,

with a brief justification for each. Firstly, it is assumed that although autosomal lethal or semilethal mutations which are sex-limited may occur, their net effect is not such as to obscure the different effects on the sex ratio of paternal versus maternal radiation. Clearly, were this not so, the deviations postulated could be altered in degree or direction depending upon the relative frequencies of male-limited or female-limited mutants, or both. In view of the current state of knowledge of radiation genetics, it seems appropriate to assume that the predominant change in the sex ratio will stem from sex-linked rather than sex-limited effects.

Secondly, it has been assumed that the effect on the sex ratio of genes in the Y-chromosome is negligible, and that there exist no homologous portions of the X- and Y-chromosomes. The reasonableness of the former is supported by the knowledge that there is known, at present, no single, well-documented case of holandric inheritance, although this form of genetic transmission should be easy to recognize [for a discussion of Y-borne inheritance, see Stern (1)]. The legitimacy of the assumption that there is no homology between the X- and Y-chromosomes rests on the cytological work of Mathey (2) and Sachs (3).

Thirdly, and with reference to the exposure of both parents, it is assumed that sex-linked recessive mutants would outnumber sex-linked dominant mutations. The only animal for which data exist relevant to this assumption is *Drosophila melanogaster*, and here sex-linked recessives are estimated to be several times more common than sex-linked dominant mutants. In this connection, however, attention must be called to the

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Table 1. Summary of the findings of Kaplan (7) and of Macht and Lawrence (6) with regard to the frequency of male births following parental exposure to ionizing radiations.

Exposed parent	Estimated dose (r)	Total offspring of known sex born after radiation	Male	Female	p
<i>Kaplan, 1956</i>					
Mother	50-200	407	200	207	0.4914
<i>Macht and Lawrence, 1955</i>					
Father	Unknown	4277	2198	2079	0.5139
None	Control	3491	1830	1661	0.5242

evidence which suggests that sex-linked spontaneous mutation occurs more frequently in the human male than in the female (4, 5). The possibility must be entertained that the same may hold true for sex-linked induced mutations. If this is, in fact, true, then maternal exposure may not lead to a relatively greater effect on the sex ratio than paternal exposure. The directions of deviation of the sex ratio would not of course be altered even if induced sex-linked mutations occurred more frequently in the male than in the female. One other assumption which has been made in the analysis of the data presented below is that the increase in gene mutations with increasing radiation is linear over the measurable range of exposures. The linearity of the response in gene mutations to dose of radiation is one of the cornerstones of radiation genetics, and rests on a literature far too extensive to review here. Suffice it to say that since linearity obtains in all organisms thus far studied, it seems improbable that a different situation would obtain in man.

### Studies of the Sex Ratio

To date, four studies on man have reported information on the sex ratio among infants born subsequent to parental exposure to ionizing radiations. These are the observations of Macht and Lawrence (6) on the offspring of American radiologists; of Kaplan (7) on the pregnancies occurring to women following the use of x-ray therapy to correct an apparent sterility; of Turpin, Lejeune, and Rethore (8) on the sex of children born to French men and women receiving x-ray therapy for sciatic neuralgia and a variety of other complaints; and, lastly, of Neel and Schull (9) on pregnancy terminations to survivors of the atomic bombings of Hiroshima and Nagasaki. We present in Table 1 a summary of the findings of Kaplan and of Macht and Lawrence; in Table 2, the findings of Turpin, Lejeune, and Rethore; and in Tables 3 and 4, the findings of Neel and Schull. In the presentation of these data, we give, when it has been published, the author's estimate of the

average exposure (or the range) sustained by the various groups of individuals. Let us be the first to recognize the tenuous nature of these estimates; however, since we shall be principally concerned with the direction of deviation of the sex ratio rather than the magnitude of the change, precise specification of the dose is less important, in a sense, than the proper ranking of the various exposure groups.

In a discussion of the data presented in Tables 1 to 4, one can deal rather briefly with the findings of Kaplan and of Macht and Lawrence (Table 1). In Kaplan's case, there does not exist a satisfactory unexposed control for his observations, nor have the data been presented in a fashion such that the proportion of male births could be regressed on different maternal exposures (generally Kaplan's cases received 200 roentgens, but some appear to have received less). In Macht and Lawrence's data, it is impossible to estimate the average exposure of radiologists in the United States as contrasted with physicians who are not radiologists. It is worth noting, however, that the direction of deviation in Kaplan's data would appear to be in keeping with genetic theory, for the frequency of male births is less than in the general population; this may not, however, be a meaningful comparison. The direction of deviation in Macht and Lawrence's data, on the other hand, is contrary to genetic theory; there are proportionately fewer, rather than more, males when the fathers were exposed.

Turpin, Lejeune, and Rethore's observations (Table 2) warrant somewhat more extended discussion. These authors selected for study, from the radiotherapy

Table 2. Summary of the findings of Turpin, Lejeune, and Rethore (8) with regard to the frequency of male births following parental exposure to ionizing radiations.

Exposed parent*	Estimated dose (r)	Reproductive performance before exposure					Reproductive performance after exposure				
		Total matings	Total children of known sex	Male	Female	p	Total matings	Total children of known sex	Male	Female	p
<i>All cases</i>											
Father (b)	Unknown	66	112	62	50	0.5536	52	96	42	54	0.4375
Father (C <sub>1</sub> )	1295	284	465	242	223	0.5204	194	275	157	118	0.5709
Father (C <sub>2</sub> )	1461	137	231	116	115	0.5022	95	130	68	62	0.5231
Mother	1360	154	236	130	106	0.5508	97	136	63	73	0.4632
<i>Only cases having children before and after exposure</i>											
Father (C <sub>1</sub> )	1295	92	150	79	71	0.5267	92	119	66	53	0.5546
Father (C <sub>2</sub> )	1461	42	67	30	37	0.4478	42	51	27	24	0.5294
Mother	1360	45	61	37	24	0.6066	45	51	26	25	0.5098

\* An explanation of the subdivisions of paternal exposure will be found in the text.

files of all the hospitals in and around Paris, 4428 individuals who had received radiotherapy between 1925 and 1952, a substantial majority having been treated between 1940 and 1952, and where the estimated skin dose was in excess of 300 roentgens. Two other restrictions were placed upon the cases to be selected—namely, the radiotherapy had to be for complaints of a noncancerous nature, and the exposed persons were to be adults less than 35 years of age, if female, and less than 40, if male. Repeated questionnaires were then sent to these individuals. In all, questionnaires were sent to 3579 males, of whom 37.4 percent (1334) responded, and 849 females, of whom 33.5 percent (284) responded. Turpin *et al.* do not present data which would afford some indication of how representative the respondents were of the whole group queried. This is, of course, a problem of real concern in all questionnaire surveys, and especially in those surveys where only a minority of those queried bother to respond.

Be this as it may, the irradiated males were divided by these authors into three groups (a) 368 cases where the x-ray was delivered high up on the lumbar region, or to the thigh, (b) 180 cases where irradiation was to the pelvic area but with the gonads probably shielded, and (c) 786 cases where the subjects were irradiated in the pelvic area under conditions making protection of the gonads impossible. Turpin *et al.* present data on reproductive performance for groups (b) and (c), but not for group (a). In the analysis of their data, group (b) is rejected because of the uncertainty regarding the amount of radiation received by the group. The third group, (c), was further subdivided into individuals treated for "sciatic neuralgia" [517 cases (group c<sub>1</sub>)], and for various other complaints [269 cases (group c<sub>2</sub>)].

Turpin *et al.* use, as is apparent from Table 2, the reproductive performance of the exposed individuals prior to their exposure as the base of reference with which to compare reproductive performance after exposure. This procedure leads to a confounding of age and parity effects with those due to radiation. The importance of this confounding is difficult to assess. We know (i) that first-born children are more frequently males than children in subsequent birth ranks (10), and (ii) that the frequency of male births tends to decrease with advancing maternal or paternal age (11). It is not clear whether the correlation between

birth rank and frequency of male births is due wholly or in part to the correlation between birth rank and parental age. Conceivably this confounding could, then, lead to an overestimation of maternal exposure effects and an underestimation of paternal effects.

The extent of this over- or underestimation is in part a matter of speculation; however, Ciocco (10) has found that the sex ratio among first born is

0.5153 and that the sex ratio among fifth or higher order births is 0.5124. This change would be the equivalent of approximately 50 rep of maternal exposure, judging from the Japanese data (see below). It is not our purpose to present a critique of the data of Turpin *et al.*, but merely to indicate that this study, like all of the others, including our own, suffers from several deficiencies. One must, therefore, exercise considerable caution

Table 3. Summary of the findings in Japan with regard to the association of the frequency of male births and parental exposure. Only one parent exposed.

Father only exposed				Mother only exposed			
Total births	Male births	p	Estimated mean exposure (rep)	Total births	Male births	p	Estimated mean exposure (rep)
<i>Neel and Schull, 1956 (1948-1953) (9), parents unrelated</i>							
31,904	16,613	0.5207	0	31,904	16,613	0.5207	0
3,670	1,892	0.5155	8	14,684	7,681	0.5231	8
839	442	0.5268	75	2,932	1,474	0.5027	75
534	284	0.5318	200	1,676	850	0.5072	200
<i>Neel and Schull, 1956 (1954-1955) (9), parents unrelated</i>							
11,640	6,067	0.5212	0	11,640	6,067	0.5212	0
1,498	774	0.5167	8	4,926	2,512	0.5099	8
387	211	0.5452	75	1,026	562	0.5478	75
219	113	0.5160	200	592	311	0.5253	200
<i>This article (1948-1953), parents related</i>							
2,622	1,396	0.5324	0	2,622	1,396	0.5324	0
295	152	0.5153	8	963	466	0.4839	8
83	46	0.5542	100	258	134	0.5194	100

Table 4. Summary of the findings in Japan with regard to the association of the frequency of male births and parental exposure. Both parents exposed.

Total births	Male births	p	Estimated mean exposure (rep)	
			Mother	Father
<i>Neel and Schull, 1956 (1948-1953) (9), parents unrelated</i>				
5994	3053	0.5093	8	8
658	337	0.5122	8	75
422	225	0.5332	8	200
703	354	0.5036	75	8
615	319	0.5187	75	75
192	94	0.4896	75	200
318	165	0.5189	200	8
145	72	0.4966	200	75
145	71	0.4896	200	200
<i>Neel and Schull, 1956 (1954-1955) (9), parents unrelated</i>				
1474	806	0.5468	8	8
220	129	0.5864	8	75
174	101	0.5805	8	200
212	111	0.5236	75	8
107	53	0.4953	75	75
66	35	0.5303	75	200
89	48	0.5393	200	8
43	20	0.4651	200	75
33	18	0.5455	200	200
<i>This article (1948-1953), parents related</i>				
394	208	0.5279	8	8
69	38	0.5507	8	100
54	29	0.5370	100	8
43	21	0.4884	100	100

in any interpretation of the data on the sex ratio. Be this as it may, it is interesting to observe that of the four comparisons afforded by all of the data presented by Turpin *et al.*, three are in the direction which one would expect on genetic grounds.

### Japanese Data

Before we turn to a description of the Japanese data, it is important that one rather important fundamental difference between the study in Japan and those previously mentioned be pointed out. The data of Kaplan, Macht and Lawrence, and Turpin *et al.* involve observations on individuals whose exposure was distributed over some interval in time. Thus Macht and Lawrence's observations are on persons whose total dose may be appreciable, but this dose was incurred at relatively low levels and over a considerable period of time. Kaplan's individuals received three exposures of 50, 75, and 75 roentgens, and the interval intervening between successive exposures was 7 days. Turpin *et al.* do not state that the individuals in their study received repeated exposures; however, if the practice of radiotherapy in France is similar to that in the United States, this is undoubtedly so. The observations from Hiroshima and Nagasaki, on the other hand, are on individuals who received but a single exposure.

In the past, this distinction would perhaps not have been considered important since the data from *Drosophila*, for example, suggest that the critical factor is the total dose and not the period of time over which this dose occurred. Recently, however, Russell (12) has presented data on the mouse which suggest that the effect of chronic irradiation for a given dose and in terms of the frequency of the induction of specific locus mutations is less than the effect of acute irradiation. Russell states "Results obtained from an accumulated dose of 600 r given to spermatogonia at approximately 100 r/wk continuous irradiation show a much lower mutation rate than that obtained earlier with a 600 r acute dose of x-rays." The same also appears to be true at a total dose of 100 roentgens. If this finding is confirmed, and if the same phenomenon holds true in man, then there are reasons for believing that the Japanese data are not comparable to the studies in the United States and France.

The Japanese data concerning the effects of radiation on the sex ratio fall into three categories, as follows, two of which (i and ii) have been presented previously (9), but analyzed differently, one of which (iii) is presented here for the first time: (i) the sex ratio in infants born to *unrelated* parents in the years 1948–1953, these infants all examined by Japanese physicians; (ii) the sex ratio in infants born to *unrelated* parents in the years 1954–1955, sex reported by the parents but not verified by a physician examiner; (iii) the sex ratio in infants born to *related* parents in the years 1948–1953, these infants all examined by physician examiners. [A description of the background of these children will be found in Schull's report (13).]

Detailed presentation of the method of data collection and the bases for the dosage estimates for the parents will not be attempted here, since this material has been described by Neel and Schull (9) and Schull (13). The present method of analysis was an outgrowth of an effort to integrate the findings on the offspring of related parents with those previously reported on the pregnancy terminations of unrelated parents. In the analysis to follow, we have treated the data as if they were the results from three separate, but similarly oriented, experiences. The decision to do this was based upon two considerations. Firstly, the information collected in the years 1948–1953 involved direct observations by physicians on newly born infants, whereas the information obtained in 1954–1955 was based upon municipal birth records supplemented by a questionnaire to the parents. The two methods of collecting data would seem sufficiently different to justify maintaining a distinction between the two bodies of data which were collected. Secondly, within the years 1948–1953, the division of the data into observations on the offspring of related and unrelated parents seems appropriate in view of the frequently voiced belief that the increased homozygosity of the inbred child may make it a more sensitive indicator of genetic damage, and direct combination of these data was not feasible because of the dissimilarity in the frequency of consanguineous marriages in the various exposure classes. Let us turn now to a brief description of how the data have been analyzed, and a presentation of the results which were obtained.

As we have indicated, we have, in ef-

fect, three experiences, and the information with respect to each of these three experiences can be further subdivided into three parts—namely, pregnancies where the mother was exposed but the father was not, where the father was exposed but the mother was not, and where both parents were exposed. Within each of these nine "experience-exposed parent(s)" groups, there exist three or more dosage levels. Thus it is possible to fit nine linear regressions of the frequency of male births on the dose of radiation received by the parent(s). Six of these regressions will be of the form

$$E(p_{ij}) = \bar{p} + b(d_i - \bar{d}),$$

where  $E(p_{ij})$  is the expected proportion of males in the  $i^{\text{th}}$  exposure class,  $\bar{p}$  is the mean proportion of males,  $d_i$  is the dose in the  $i^{\text{th}}$  exposure class,  $\bar{d}$  is the average dose, and  $b$  is the regression coefficient. Three of the regressions will be of the form

$$E(p_{ij}) = \bar{p} + b_1(F_i - \bar{F}) + b_2(M_j - \bar{M}),$$

where  $b_1$  and  $b_2$  are now partial regression coefficients,  $F_i$  and  $M_j$  are, respectively, the doses in the  $i^{\text{th}}$  paternal and  $j^{\text{th}}$  maternal exposure groups,  $\bar{F}$  and  $\bar{M}$  are the mean paternal and maternal exposures, and  $\bar{p}$  is, again, the mean proportion of male births. The regressions which were, in fact, fitted were weighted to allow for the differences in the numbers of observations at the various exposure levels. The weights which were used were the reciprocals of the variances (the information) of the proportions of males at the different dosage levels. The final weights were obtained by iteration, starting with the observed proportions as trial values. The intercepts and regression coefficients which were obtained are presented in Table 5. Several comments on these values are in order.

1) It should be noted that no less than 11 of the 12 regression coefficients are of the sign anticipated by genetic theory—that is to say, the deviation is in the direction anticipated if sex-linked mutations have been induced by the exposure. The one nonconforming coefficient is that for mothers unrelated, 1954–1955. The prior probability that 11 or more of 12 regression coefficients will have signs in keeping with genetic theory, if the signs of these regression coefficients are, in fact, equiprobable, is approximately 1 in 341. Clearly the array of signs is significant.

2) Only one of the regression coefficients can be shown to be significantly different from zero, at the 5-percent level of significance, and, unfortunately none of the common regression coefficients for mothers only exposed, fathers only exposed, or both parents exposed differs significantly from zero. It should be mentioned here that substantially the same results are obtained if the arc sin transformation is used.

3) It will be noted from Table 3 that certain observations—namely, those where both parents were unexposed—occur more than once. This, of course, implies that the regression coefficient for “fathers only exposed, 1954–1955,” say, is not wholly independent of the regression coefficient for “mothers only exposed, 1954–1955.” It may, therefore, be argued that we are not, in fact, dealing with 12 independent regression coefficients since some data are scored twice. This difficulty can be avoided, at the expense of some observations, by omitting entirely the observations on both parents unexposed, and basing the regression coefficients on only those data where the “exposed” parent experienced some irradiation. When this is done, we find that 10 of these 12 estimates have the signs one would expect from genetic theory under these circumstances. A simple sign test reveals that approximately 2 times in 100 we would expect this distribution of signs, or one favoring genetic theory even more if, in fact, the null hypothesis were true.

### Analysis

The findings in the Japanese data pose two very interesting and important questions. (i) How much confidence can we place in these findings as evidence of radiation-induced genetic damage? (ii) If the changes in the sex ratio are, in fact, manifestations of genetic damage, why do we not find evidence for a radiation-induced change in the frequency of congenital malformations or one of the other attributes of a pregnancy termination? In this connection, it should be stated that an analysis of radiation effects in the consanguineous material with respect to malformation frequency and frequency of stillbirths and neonatal deaths, to be presented in detail elsewhere, fails to yield results comparable to those regarding sex ratio, in their negativity confirming the findings reported earlier for the children born to

Table 5. Means and regression coefficients obtained by fitting a weighted linear regression of the proportion of male births to average group exposure in the Japanese data. The values in parentheses are those obtained when unexposed parents are rejected.

References: Neel and Schull, 1956 (9); Schull and Neel, 1958 (this article)	Father only exposed		Mother only exposed		Both parents exposed		
	$\bar{p}$	b*	$\bar{p}$	b	$\bar{p}$	b	
1948–1953							
Unrelated parents	0.5202	0.0058 (0.0094)	0.5213	-0.0101† (-0.0111)	0.5102	0.0039 (0.0047)	0.5102 -0.0037
Related parents	0.5307	0.0188 (0.0423)	0.5204	-0.0116 (0.0386)	0.5310	0.0024 (0.0141)	0.5310 -0.0179
1954–1955							
Unrelated parents	0.5211	0.0039 (0.0047)	0.5186	0.0090 (0.0141)	0.5464	0.0137 (0.0080)	0.5464 -0.0269
Common regression coefficients		0.0056		-0.0080		0.0036	-0.0042

\* Regression coefficients are given as increase or decrease in proportion of male births per 100 rep.

† Significant at the 5-percent level.

unrelated parents (9). Clearly a categorical answer to either of these questions is impossible; however, certain observations seem pertinent to any answer which one may arrive at.

With respect to the first of these two questions, we have indicated elsewhere (9) the interpretive difficulties which arise when one begins to select, in the Japanese data, specific cells or groups of cells on which to base comparisons. The present approach would, however, seem to avoid many of these difficulties since (i) all of the data are used, and (ii) the division of the data was based upon a priori considerations regarding parental exposure, relationship, and method of data collection alone, and did not involve value judgments regarding the extent to which one portion of data, collected at one time and in one manner, was *in pari materia* with another collected at the same time and in the same manner.

It must be pointed out, however, that the sex ratio, as a variable, leaves much to be desired, the elegant genetic argument which can be advanced for expecting changes in the sex ratio consequent to parental exposure notwithstanding. Any number of factors—for example, maternal age, paternal age, parity, war, and so forth—seem capable of altering the sex ratio, and though these effects are, in general, small, adequate explanation for the peculiar variations which occur due to these factors has not been advanced. Perhaps the greatest recommendation for accepting the observations with regard to the sex ratio as a manifestation of a real effect of parental exposure is the consistency of the findings. It is true, however, that one does not find within the Japanese data other evidence of sex-linked lethal genes which might logically be expected, such as an

increase in the difference in frequency between inviable males and inviable females as maternal exposure increases. The significance of this absence of what might be termed “secondary effects” is not readily appraised since (i) the direct effect on the sex ratio is itself small and (ii) the sex difference in viability has been measured only for the period from approximately the 21st week of gestation onward. Thus, sex-linked lethal mutants leading to gametic death or to the early death of the zygote would not come within our ken.

A further possible recommendation for accepting the results as real is the apparent “reasonableness” of the change. The following rather simple calculation illustrates this: The average number of induced sex-linked lethal mutants at any given dose of radiation is equal to the product of the number of genetic loci at risk, the probability of inducing a mutant per unit dose, and the dose received. If we accept 0.0060 as the best estimate of the change in the sex ratio following 100 rep of maternal irradiation, and if we assume that the number of “targets”—that is, sex-linked lethal producing genetic loci on one X-chromosome—lies between 250 and 2500, then we find that the probability of a sex-linked lethal mutation per rep lies in the interval  $2.4 \times 10^{-7}$  and  $2.4 \times 10^{-8}$ . Current genetic thinking would tend to suggest that the number of loci at risk is rather nearer 250 than 2500, and hence that the sensitivity of human genes would be more likely to be of the order of  $2.4 \times 10^{-7}$ , a figure which agrees well with the findings for the only other mammal studied thus far, the mouse (14), but which suggests a significantly greater sensitivity than that observed in *Drosophila*.

With respect to the second of the two questions raised above, concerning the

implications for the validity of the sex-ratio findings of the failure to demonstrate parallel changes with regard to the frequency of malformations or stillbirths or neonatal deaths, it should be pointed out that Neel (15) has recently suggested, on the basis of an analysis of certain aspects of the Japanese data and a comparison of the findings with those available for Caucasian populations, that a significant fraction of congenital malformations may be the segregants from complex homeostatic genetic systems. If this viewpoint is correct, then it follows that induced mutations at loci involved in these homeostatic systems, while ultimately resulting in an increase in malformation frequency, would not be expected to bear the same simple and immediate relationship to malformation frequency as sex-linked lethal mutations do to the sex ratio. It may well be, then, that no conflict of evidence is involved

in the failure to demonstrate an effect of radiation exposure on malformation frequency in the first postbomb generation.

### Summary

An analysis of new data concerning the sex of children born to the survivors of the atomic bombings of Hiroshima and Nagasaki, together with a reanalysis of the data previously presented by Neel and Schull (9), reveals significant changes in the sex ratio of these children, changes in the direction to be expected if exposure had resulted in the induction of sex-linked lethal mutations (16).

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## News of Science

### Role of Director of Defense Research and Engineering under the Department of Defense Reorganization Act

One of the elements of the Department of Defense Reorganization Act (now signed into law by President Eisenhower) that has brought forth little criticism from opponents of the bill is that calling for the appointment of a "Director of Defense Research and Engineering." In his message to Congress of 3 April, the President, pointing to the history of interservice rivalries in the research field, the intensification of these conflicts in recent times, particularly in regard to missile development, and the folly implicit in tolerating "this unwise service competition in this critical area," offered the following solution:

#### President's Request

"To give the Secretary of Defense the caliber of assistance he requires in the research area, I recommend that the new position of Director of Defense Research and Engineering be established in place of the Assistant Secretary of Defense for

Research and Engineering. I believe his salary should be equal to that of the secretaries of the military departments. He should rank immediately after the service secretaries and above the defense assistant secretaries. As the principal assistant to the Secretary of Defense for Research and Development, he should be known nationally as a leader in science and technology. I expect his staff, civilian and military, also to be highly qualified in science and technology. This official will have three principal functions: first, to be the principal adviser to the Secretary of Defense on scientific and technical matters; second, to supervise all research and engineering activities in the Department of Defense, including those of the Advanced Research Projects Agency and of the Office of the Director of Guided Missiles; and, third, to direct research and engineering activities that require centralized management. Further, it will be his responsibility to plan

research and development to meet the requirements of our national military objectives instead of the more limited requirements of each of the military services. It is of transcendent importance that each of our principal military objectives has strongly and clearly focussed scientific and technical support.

"With the approval of the Secretary of Defense, this official will eliminate unpromising or unnecessarily duplicative programs and release promising ones for development or production. An especially important duty will be to analyze the technical programs of the military departments to make sure that an integrated research and development program exists to cover the needs of each of the operational commands. It will be his responsibility to initiate projects to see that such gaps as may exist are filled. In addition, the director will review assignments by the military departments to technical branches, bureaus and laboratories to assure that the research and engineering activities of the Defense Department are efficiently managed and properly coordinated. I would charge the director, under the direction of the Secretary of Defense, with seeing that unnecessary delays in the decision-making process are eliminated, that lead times are shortened, and that a steady flow of funds to approved programs is assured. Only under this kind of expert, single direction can the entire research and engineering effort be substantially improved. In these various ways, he should help stop the service rivalries and self-serving publicity in this area."

### Congressional Response

The act fulfills all of the requirements of the President's message in this matter. It lists the three functions of the Director of Defense Research and Engineering as the President had enumerated them, and implies others about which he had been specific. The full meaning and intent of the President's recommendations are realized in the act.

### Changes Effected

Two major significant changes are effected by the Reorganization Act in the matter of military research. The first is one of status. Appointment of a Director of Defense Research and Engineering reflects the formal recognition of science's critical role in the military. The Committee on Armed Services of the House, chaired by Carl Vinson, put its views in this way in a committee report: "From the testimony presented, and from prior hearings on the subject of research and development, the committee is of the firm opinion that the Secretary of Defense has need for a principal assistant on scientific and technical matters. The research and engineering activities of the Department have become so extensive and varied in nature as to require a director whose sole function is to perform overall supervision of those activities and to direct and control those which the Secretary considers to require centralized management. The responsibilities of the Director of Defense Research and Engineering will be of such far-reaching importance to the Department as a whole that the committee feels he should be a member of the Armed Forces Policy Council, and have so provided in this legislation." The importance of the position is further emphasized by the adoption of the President's recommendation that the new Director should rank above the Assistant Secretaries of Defense, and should receive compensation equivalent to that of the Secretaries of the services.

### Advance Research Projects Agency

A second major change is that which affects the Advanced Research Projects Agency (ARPA). The bill deletes from section 7 of the Act of 12 February 1958 the authority for the Secretary of Defense, or his designee, to contract for research and development work. The intent of this change is to take away from the Advanced Research Projects Agency the authority to enter into research and development contracts, since the Director of Defense Research and Engineering will supervise the Advanced Research Projects Agency and can receive the necessary power to contract by delegation from the Secretary of Defense.

As it would appear now, before the

Reorganization Act goes into effect and the all-important question of who will take the post of Director of Defense Research and Engineering is decided, the main effect of the provisions concerning the Advanced Research Projects Agency will be a matter of the channeling of funds. The function of the agency has not been altered; only the route by which it receives its appropriations. The man occupying the post, one "known nationally as a leader in science and technology," if the President's specifications are met, would presumably be well inclined toward the aims of the agency—research and developments with regard to advanced space projects—and, with the new power of his position, would be able to aid in their achievement to a greater degree of effectiveness than the now existing Assistant Secretaries of Defense for Research and Engineering.

A second possible change concerning ARPA involves an eventual shift of certain aspects of its work to the office of the Director of Defense Research and Engineering. In report 1765 of the House Armed Services Committee, quoted above, the following statement appears: "The committee recognizes that the Advanced Research Projects Agency will continue to have authority to engage in advanced space projects until 12 February, 1959, unless otherwise restricted by law or by the direction of the Secretary of Defense. At the same time, it recognizes that some such projects will be of primary military significance and that some provision must be made for continued military participation in this area. Therefore, in section 9 of the bill, the Secretary of Defense or his designee, subject to the approval of the President, is authorized to engage in basic and applied research projects essential to military requirements. It is intended by these provisions to authorize the Secretary of Defense, or his designee, to engage in outer space projects beyond February 12, 1959, if such projects have primary military significance, and are not precluded by law and are approved by the President."

This shift of essentially military projects from the Advanced Research Projects Agency to the Director of Defense Research and Engineering is accomplished by the relevant deletion in the legislation establishing ARPA and the inclusion in the new bill of the provision: "The Secretary of Defense shall assign any weapons system to such military department or departments for production and operational control as he may determine."

### Benefits of New Position

The establishment of the position of the Director of Defense Research and

Engineering under the Department of Defense Reorganization Act of 1958 accomplishes three major ends which are designed to ameliorate the conditions under which the department's scientific activity is carried on. The first aim is consolidating and streamlining. The responsibilities for research are brought together in one post. The person filling this post would serve as the "principal assistant on scientific and technical matters" to the Secretary of Defense. Research and development projects which have primary significance in their military applications would come under his control and funds for these projects would be channeled through him from the Secretary of Defense.

To emphasize his role, and through it, the role of science and technology in the nation's defense activity, the Director of Defense Research and Engineering is given the two prestige marks requested by the chief executive—rank above the Assistant Secretaries of Defense and compensation equal to that of the Secretaries of Army, Navy, and Air Force.

And lastly, he is given specific authority to "direct and control research and engineering activities that the Secretary of Defense deems to require centralized management."

By these means, the Director of Defense Research and Engineering should have the position, the prestige, and the explicit authority to control from a superior position the scientific and technical projects of the Department of Defense, to establish, fund, and direct them with a freedom of action and directness of delegation hitherto unattainable.

### Explorer IV

The United States launched its fourth and heaviest satellite—38.43 pounds—on 26 July. Explorer IV (1958 Epsilon) is designed for an intensive study of corpuscular radiation in space as part of the International Geophysical Year program. It is the first of this country's satellites to be launched in a northern direction from the Missile Test Center at Cape Canaveral, Fla., and it will report information from higher latitudes not previously explored by U.S. satellites.

Explorer IV was put in orbit by a Jupiter C launching vehicle developed jointly by the Army Ballistic Missile Agency and the California Institute of Technology Jet Propulsion Laboratory. The four-stage Jupiter C missile also was used to launch Explorers I and III [Science 127, 330 (14 February 1958)]. The new satellite circles the earth in 110.224 minutes, with a apogee of 1379.8 statute miles and a perigee of 157.3.

Explorer IV is heavier by 7 pounds than I and III, but identical in size and configuration (80 inches long). Earlier temperature and micrometeorite experiments have been eliminated in favor of four separate cosmic ray detectors that will provide the most detailed radiation data yet obtained by a U.S. IGY satellite. The added weight is in instrumentation and was made possible by improvements made at the Jet Propulsion Laboratory in the solid fuels in the two upper stages of the Jupiter C missile.

Launching was made in a northeast direction, which took the satellite on its first pass along the eastern coast of the United States and Newfoundland, over England, central Europe, southern Russia, India, Australia, and up across the Pacific Ocean and the United States.

The new orbit will take the satellite up to approximately 51 degrees north latitude. Earlier Explorers had not gone farther north than 35 degrees. This means that Explorer IV's orbit is over areas of greater population than were the paths of Explorers I and III.

The Jet Propulsion Laboratory's contributions to the Explorer IV project were directed by J. E. Froelich. He works under William H. Pickering, laboratory director.

JPL's responsibility in the Explorer IV program included development of the three upper high-speed stages, the low-power radio beacon and subcarrier oscillators, fabrication of the steel shell of the satellite, except the nose cone which was produced by the Army Ballistic Missile Agency. The Pasadena laboratory, ABMA, Army Ballistic Research Laboratory, Aberdeen, Md., and the Army Signal Corps cooperated in establishing and operating the Microlock ground radio network. The Microlock system was developed by JPL.

The radiation package was developed by James A. Van Allen's physics department at the State University of Iowa at the request of the satellite panel of the National Academy of Sciences IGY Committee. The Naval Research Laboratory provided the high-power beacon, and the Army Signal Corps supplied the battery packs.

The satellite carries two Geiger-Mueller tubes and two scintillation counters to measure cosmic ray intensities. One of each is shielded to eliminate data below certain energy levels, and the unshielded scintillation counter's data is directed into two radio channels reporting different levels of energy. This gives ground radio stations five channels of information.

Explorer IV thus will handle not only a far greater range of cosmic ray data, but will break the information down into levels of intensity. Previous satellites re-

ported only the gross amount of radiation they encountered.

This means that Explorer IV will be able to differentiate between the energy levels of the cosmic rays that strike its counters. The data will show not only the total number of particles but also what fraction of this total falls within certain preselected energy ranges.

For example, Explorers I and III showed a counting rate of more than 20,000 counts per second in the high-altitude portion of the orbit. It is suspected that only a small fraction, about one-tenth of 1 percent, of this total was caused by those high-energy particles which physicists have seen before and identified as cosmic rays. This suspicion implies that almost all of these particles were of a new low-energy type.

However, since Explorers I and III could not differentiate between energy levels, this suspicion could neither be proved nor disproved. Now in Explorer IV the shielded counters will respond only to the high-energy particles, while the unshielded counters will see everything. Furthermore, the unshielded scintillation counter will be provided with special pickups which can further differentiate between energy levels.

Both the high-power and low-power radio beacons will transmit continuously for an expected life of 2 months. The low-power beacon radiates 10 milliwatts of energy. The low-power beacon will be used mainly for tracking, but it will also report the same data as the high-power transmitter. The high-power transmitter radiates 30 milliwatts.

Explorer IV carries no tape recorder such as that in Explorer III. Decision to devote the entire payload to cosmic ray studies was made after the instruments in the first two Explorers were swamped at times by the unexpected intensity of cosmic ray activity in space.

## Space Science Board

The National Academy of Sciences-National Research Council has announced the formation of a 16-man Space Science Board, "to survey in concert the scientific problems, opportunities and implications of man's advance into space." Lloyd V. Berkner, president of Associated Universities, Inc., and president of the International Council of Scientific Unions, has been appointed chairman.

Named as executive director of the new board was Hugh Odishaw, who also serves the Academy-Research Council as executive director of the U.S. National Committee for the IGY. A permanent staff will be recruited to serve as a secretariat.

The board, besides acting as the focal point for all Academy-Research Council activities connected with space-science research, will coordinate its work with appropriate civilian and government agencies, particularly the National Aeronautics and Space Administration [*Science* 128, 290 (8 August 1958)], the National Science Foundation, and the Advanced Research Projects Agency (see lead news article, this issue), and with foreign groups active in this field.

The functions of the Space Science Board will include studies of research opportunities and needs opened up by the advent of modern rocket and satellite tools, advice and recommendations on space science to interested agencies and institutions, stimulation of research interest in the rocket and satellite fields, and cooperative activities in this area with academies and similar institutions abroad.

Eleven ad hoc committees have already been organized to carry on the work of the board. These committees, together with their chairmen and vice chairmen (who comprise the membership of the board), follow:

1) Geochemistry of Space and Exploration of Moon and Planets—chairman, Harold C. Urey, professor of chemistry, University of California, La Jolla; Vice Chairman, Harrison S. Brown, professor of geochemistry, California Institute of Technology.

2) Astronomy and Radio Astronomy—chairman, Leo Goldberg, chairman of the department of astronomy, University of Michigan.

3) Future Vehicular Development (beyond vehicles immediately available and including possible space stations and interplanetary vehicles for scientific research)—chairman, Donald F. Hornig, professor of chemistry, Princeton University.

4) International Relations Field (coordination with International Council of Scientific Unions and other national scientific bodies on problems in international sharing of payloads, international cooperation in space activities, and advice on the formulation and effects of regulatory policies)—chairman, W. A. Noyes, dean of the College of Arts and Science, University of Rochester.

5) Immediate Problems (space laboratories, orbits, currently feasible research projects, and liaison with the Technical Panel on the Earth Satellite Program of the U.S. National Committee for the International Geophysical Year during terminal phases of IGY)—chairman, R. W. Porter, chairman of the USNC-IGY Technical Panel on the Earth Satellite Program, and consultant (communication and control) Engineering Services, General Electric Company, New York.

6) Space Projects (analysis of advanced space research proposals and long-range planning)—chairman, Bruno B. Rossi, professor of physics, Massachusetts Institute of Technology.

7) Ionosphere (experiments pertaining to auroral and ionospheric effects, including whistlers and special propagation phenomena)—chairman, A. H. Shapley, physicist, National Bureau of Standards, Boulder, Colo.

8) Physics of Fields and Particles in Space—chairman, John A. Simpson, professor of physics, University of Chicago; vice chairman, James A. Van Allen, head of the department of physics, Iowa State University.

9) Future Engineering Development Beyond Available Facilities (telecommunications, telemetry, guidance, environmental conditions, and advanced laboratory requirements)—chairman, O. G. Villard, Jr., professor of electrical engineering, Stanford University.

10) Meteorological Aspects of Satellites and Space Research—chairman, Harry Wexler, director of meteorological research, U.S. Weather Bureau.

11) Psychological and Biological Research—chairman, H. Keffer Hartline, biophysics section, Rockefeller Institute for Medical Research; vice chairman, S. S. Stevens, professor of psychology, Harvard University.

A twelfth committee, on geodesy, will be chaired by a board member still to be selected.

## Soil and Water Conservation

The U.S. Department of Agriculture has announced the appointment of a working group to study the need for facilities for research in soil and water conservation. The study is being made at the request of the Senate Committee on Agricultural Appropriations. Members of the working group are G. M. Brownning of Iowa State College, representing the state agricultural experiment stations; Gerald E. Ryerson of the Soil Conservation Service; and Cecil H. Wadleigh and Darnell M. Whitt of the Agricultural Research Service.

The group will receive recommendations from federal, state, and local organizations concerned with the conservation of soil and water resources. Those interested are invited to present their evaluation of the kind and extent of soil and water problems needing research. A series of public hearings is planned. To make a presentation at these hearings, a written request should be submitted before 29 August to the secretary of the working group, Dr. Darnell M. Whitt, Plant Industry Station, Beltsville, Md.

The new study will provide an esti-

mate of (i) total soil and water conservation research needs with respect to problems of regional and national significance, (ii) the capacity of existing research facilities to meet those needs, and (iii) the need for any additional research facilities. Representatives of federal, state, and local agencies concerned with soil and water resources are expected to present material for consideration. The working group is planning to complete its study and make its report to the Secretary of Agriculture on or before 31 December 1958.

## French Science Association

The French Association for the Advancement of Science (Association Française pour l'Avancement des Sciences) met at Namur, Belgium, 15–22 July. The program allowed time not only for the regular sessions at which scientific papers were read, but also for several trips to places of special interest: archeological sites in Namur, the Belgian littoral, the Brussels' exposition, and the Ardennes region. Major addresses were given by Dr. Cox, who spoke on the advances in astronomy since publication of *Traité du ciel*, and by M. Laffineur, director of the Radioastronomy Laboratory of the Institute of Astrophysics in Paris, on radioastronomy.

Wallace Brode, president of the American Association for the Advancement of Science and science adviser to the Secretary of State, represented the AAAS at the annual banquet at which J. Peres, president of the French association and dean of the faculty at the University of Paris, presided.

## Scientists in the News

GLENN T. SEABORG, Nobel laureate and professor of chemistry at the University of California, Berkeley, assumed the chancellorship of the Berkeley campus on 15 August. He succeeds CLARK KERR, who became president of the university on 1 July. Seaborg will continue in his position as associate director of the Radiation Laboratory.

HARALD T. FRIIS of Rumson, N.J., the electrical engineer who set up the receivers in England for the radiotelephone system that connected America and Europe in 1923, will receive the Franklin Institute's Stuart Ballantine Medal on 15 October. A consulting engineer, formerly director of research in high frequency and electronics for Bell Telephone Laboratories, Friis is being honored for "his many important contributions to the science of radio-com-

munications during a lifetime of consistently productive research in this field, through which this science has been so notably advanced."

WAYNE C. HALL, professor of plant physiology at the Agricultural and Mechanical College of Texas, has been appointed head of the college's department of plant physiology and pathology.

DAVID M. YOUNG, JR., head of the mathematical analysis department at the Ramo-Wooldridge Corporation computation and data reduction center in Los Angeles, Calif., has been named professor of mathematics at the University of Texas and first director of the university's new Computation Center, effective next month.

WILLIAM L. DOYLE, chairman of the division of biological sequence in the department of anatomy at the University of Chicago, has been named associate dean of the Division of Biological Sciences in charge of nonclinical affairs. He succeeds the late Merle C. Coulter.

HILGARD O. STERNBERG, professor of geography at the University of Brazil, Rio de Janeiro, and director of the Center for Research in Geography of Brazil, will spend the second semester of the academic year 1958–59 at Indiana University as visiting professor of geography.

HAROLD A. BOLZ has been appointed dean of Ohio State University's College of Engineering. Associate dean of the engineering college since joining the Ohio State staff in 1954, Bolz was named acting dean last March when GORDON B. CARSON, former head of the college, was made the university's vice president, business and finance. Bolz also was given the title of director of the Engineering Experiment Station. He retains a professorship in the department of mechanical engineering.

JOHN F. DASHIELL, Kenan professor emeritus of psychology at the University of North Carolina, has been appointed by the John Hay Whitney Foundation to a visiting professorship at Wake Forest College, where he is to advise in the organization of a new independent department of psychology.

CHESTER A. SWINYARD, former medical director of the Rehabilitation Center at the University of Utah College of Medicine, has been appointed associate director of the Children's Division of New York University–Bellevue Medical Center's Institute of Physical Medicine and Rehabilitation.

## Book Reviews

**No More War!** Linus Pauling. Dodd, Mead, New York, 1958. ix + 254 pp. \$3.50.

This is a tract for the times. The "message of this book," to quote from Pauling's preface, is that "the future of the human race depends upon our willingness to cooperate, to work together in a worldwide attack on the great world problems." This is a message with which it is not easy to disagree, but one should note that "our" refers to the whole human race and not just to the American or free-world subspecies of that race.

After sounding the clarion call of "No more war!" in his opening chapter, Pauling, in the body of his book, sets forth "the facts" regarding fallout and the effects of radiation on heredity and disease. I shall not, as a person untrained in the physical sciences, attempt to pass judgment on the accuracy or balance of Pauling's summary for a lay reader of "the facts," or on the fairness of his presentation of the scientific views of those, particularly those connected with the Atomic Energy Commission, with whom he disagrees. "On these basic facts," Pauling quotes J. Laurence Kulp, on the views of Pauling and Libby on radiation, "all are agreed" (page 113). Amen. It is when one asks what the facts mean and to what extent one can read public policy directly from the contemplation of these facts, and these facts alone, that basic agreement ceases.

To Pauling, the facts mean that the testing of nuclear weapons must stop and can stop now on the basis of a readily negotiated agreement between the Soviet Union and the United States. They mean, further, that a great World Peace Research Organization should be set up within the framework of the United Nations. Given the all-round "willingness to cooperate" mentioned in the preface, the findings of this organization would presumably be accepted by acclamation.

As for the international "first-step" disarmament agreement, Pauling twice suggests (pages 184 and 190) that the Soviet Union has already accepted the plan for cessation of bomb tests with enforcement to be based on internal inspection stations. He suggests (page 185) that progress toward disarmament broke down in

1957 because Secretary Dulles intervened in the negotiations then being conducted in London by Harold Stassen. It was Dulles' "failure to reach a compromise" that "was an important factor in causing the conference to end."

Another important factor may possibly have been the Soviet delegation's failure to reach a compromise. The "we" who must be willing to cooperate includes both "us Americans" and "them Russians." The Soviet Union's peremptory rejection of the "keyhole" area-of-inspection proposal in April 1958 is only one of the more recent examples of Soviet behavior which remind us that it takes two to fail to reach a compromise—unless one is counseling his own side to surrender.

Pauling's other proposal—to bring an end to war by creating a great research organization—is not new. I do not know whether official sponsorship by the United Nations would make objective research harder or easier. It would be interesting to have testimony from the staffs of our great American foundations as to how much their programs for research on peace are now hampered by lack of funds on a scale which only governments or international organizations can provide.

There are some broad fundamental questions which Pauling's book raises but which it does not really answer; for instance:

1) Ought or ought not the United States, in the name of morality, simply cease bomb testing forthwith, whether or not there is Soviet agreement to accept international inspection, and even if indications were that such voluntary cessation would reduce the chance that the Soviet Union would later agree to effective internal inspection?

2) How does one equate the long-run biological risk of continued bomb testing and the short-run biological (and political) risk of two-way atomic war that would be involved in either a one-sided relaxation of the present effort to deter attack or an international agreement so loosely drawn as to permit unilateral violation?

3) How does one equate the gains from delayed international agreement, based on a more carefully negotiated in-

spection scheme covering a wider range of prohibited actions, and an immediate agreement calling for less stringent or narrower inspection? [For some recently published evidence as to the feasibility of a wider system of inspection, see *Inspection for Disarmament*, Seymour Melman, Ed. (Columbia University Press, New York, 1958).]

4) More broadly, what combination of firmness and conciliation in dealing with the Soviet Union will produce optimum relief from the threat of two-way thermonuclear war?

Between the Scylla of intransigence and the Charybdis of surrender, the passage is not clearly marked. The way may be narrow, tortuous, and hard to find. Faith in the brotherhood of man and a burning sense of urgency based on a knowledge of the evil effects of nuclear explosions may indicate the ultimate goal, but they are no guarantee against shipwrecks along the way. Patient analysis, as well as reliance on other kinds of skills and other kinds of facts, is needed if short-run and middle-run policies are to achieve long-run goals.

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**Obok.** A study of social structure in Eurasia. Elizabeth E. Bacon. Viking Fund Publications in Anthropology, No. 25. Wenner-Gren Foundation, New York, 1958. xv + 235 pp. Maps and tables. \$4.00.

In 1938–39 Elizabeth E. Bacon, presently professor of anthropology at Washington University, St. Louis, did field work among the Hazara "Mongols" in Iran and Afghanistan. When she began to write the present monograph in 1947, she ran into a now familiar problem. The language of anthropology, notoriously unsatisfactory, is particularly deficient when it comes to such terms as *clan*, and Dr. Bacon joined those who wished to distinguish the varieties of unilinear organizations under discrete headings, thereby separating functionally dissimilar institutions which had previously been confused because of certain superficial resemblances. Dr. Bacon employs the word *obok*, which is Mongol and means "tribal genealogical [unit]." By comparative analysis, she seeks to establish *obok* as the basic extended social group throughout Eurasia, from Britain (Scots and Welsh) to the Pacific (China).

Dr. Bacon has done an enormous amount of work in assembling data on the social organization and kin terminologies of 15 cultures in Europe and Asia, and she is to be complimented upon

making her data available in concise form. There is not space here, nor do I feel competent, to assess her treatment of the Mongol data, yet certain lacunae are strangely apparent. For example, the general tone of *Obok* makes it appear that the first florescence of political sophistication in Central Asia is that associated with Chinggis Khan, for there is no mention whatsoever of the Hsiungnu, or even the Khitan. Another gap concerns Dr. Bacon's working bibliography; this, unfortunately, is only one of many bibliographical lapses. It concerns the absence of any treatment on Dr. Bacon's part of certain significant analyses of Central Asian societies. This is particularly evident in her neglect of Krader's work on the ecology of Central Asian pastoralism and on the principal institutions of steppe society.

Just as conspicuous is Dr. Bacon's general failure to treat her major theoretical problem in the context it deserves. One gets the impression that she worked in a kind of vacuum, isolating herself from the advances that were being made in the same problem area by her colleagues in the United States and abroad. She seems unaware that the Kirchhoff work to which she refers was done, not after her field work, but in 1935, several years before! She also seems not to know that Raymond Firth struggled with the same general question at about the same time that Kirchhoff picked it up, and that Firth continues to give it considerable attention. The result of this approach is a somewhat anachronistic treatment. One simply cannot adopt Robert Lowie's position on *clan* as it was expressed in *Primitive Society* (1920) without encountering serious difficulty. As an illustration, consider Dr. Bacon's frequent assertion that in clan organization descent is traced through one parent to the total neglect of the other, a view that has been moribund for more than two decades since its exposure by Rivers and Radcliffe-Brown.

It is also strange that the obviously "Omaha" features of many Central Asian kin terminologies are never identified as such but are called "step-stair" instead. While the term introduced by Dr. Bacon is nicely descriptive, it fails to associate these Asian kin terminological features with their American counterparts. It is interesting that, despite Dr. Bacon's acceptance of the relation between *obok* and Omaha kin terminology, the Omaha terminologies in the New World correlate with classic clan organization.

Were more space available, I should like to take up Dr. Bacon's treatment of Chinese society, which seems to represent a microcosm of the defects of her whole work. To define the *chia* as a

joint family is clearly an error; and to analyze the basic Chinese familial pattern as a joint one is to compound that error. To make the *tsu* so central an institution misses the point of a large volume of recent contributions to the subject. One looks in vain in Dr. Bacon's sources for such names as Fei, Hsu, and Lang. She would have profited by consulting them.

Dr. Bacon has joined the lists in tilting with a problem of great theoretical significance and broad interest. Her treatment, though a welcome contribution, is marred with faults.

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**Physics of Fission.** Soviet Journal of Atomic Energy, Suppl. No. 1. S. M. Popova, Technical Ed. Consultants Bureau, New York, 1957. 140 pp. \$30.

In the present days of international rivalry in science, one of the interesting aspects of a book such as this is the opportunity it affords for comparing the present state of research in nuclear physics in the Soviet Union with that of the Western world. Only an incomplete comparison can be made on the evidence of this volume, both because the field is restricted and because at least seven of the 12 papers are more in the nature of surveys than presentations of original work. The survey papers accomplish their purpose excellently; B. T. Geilikman's leading paper on the "Theory of nuclear fission," A. N. Murin's paper on the "Fission products," V. N. Mekhedov's comprehensive treatment of "Spontaneous fission," and the summary of "Photofission" by L. E. Lazaeva and N. V. Nikitina all show easy scholarship and an encompassing knowledge of the literature. These essays are valuable today despite the lapse of time between the date of writing (January 1956) and that of their publication in English, and they will retain their value as stimulants for further experimentation and theoretical probing.

When one turns attention to the original research reported in this collection, a sharper comparison between East and West becomes possible. There are two documents of the Western world which are comparable in many respects, for, like the Soviet collection, they are derived from conferences related to the physics of fission, and they are not very different in date. One is the *Proceedings of the Symposium on the Physics of Fission held at Chalk River, Ontario, May 14-18, 1956* and the other is the *Proceedings of the Tripartite Conference on Cross Sections of Fissile Nuclei*,

which took place at Harwell, England, in July 1956. These documents show a great richness and variety in the Western research on fission, which one would judge to be largely missing in the U.S.S.R. if the present sample is at all comprehensive. The Russian articles on "Fission at low and high excitation energies," by N. A. Perfilov, and on "Fission by high-energy protons," by N. S. Ivanova, represent capable work and show that the Russians are making effective use of their 660-Mev synchrocyclotron. Both reports are founded upon work with photographic emulsions, and the third major original paper, on the "Determination of the threshold for emissive fission," by V. P. Shamov (which, incidentally, shows that unclear writing is no respecter of iron curtains) is likewise founded upon emulsion work. These, with some shorter notes on theoretical aspects, complete the present volume and present a contrast to the American-Canadian-United-Kingdom reports, which are founded upon all kinds of time-of-flight devices, nuclear reactors, electrostatic generators, cyclotrons, and synchrocyclotrons, together with a host of sophisticated electronic gear. The evidence seems to say that, although the Soviet research is done by expert and able men, the Western research is done by a much larger number of expert and able men. One wonders whether this will still be true 10 or 20 years from now.

The translation of the present volume is more literal than literary; it is adequate for its purpose, and the English is sufficiently clear, although it is often graceless and blunt. A few mistakes in translation are evident, the most glaring of which is in the title "Neutron fission," heading an excellent article by B. G. Erozolimskii; obviously "Fission neutrons" was the author's intent. Another occurs in A. N. Murin's survey paper entitled "The mass and charge of fission fragments," where the term *slow neutrons* is given in place of *delayed neutrons*—a considerably different concept. The most severe indictment of the present volume, however, is its price; not a few recipients will be disillusioned to find that they have bought a paper-bound volume much like a rather tawdry version of many government and laboratory reports, with an unjustified right-hand margin and a singularly tasteless treatment of the tables and figures. Prospective purchasers should be informed that the same material is available in better translation and in attractive, hard-cover book form from Pergamon Press, under the title *Physics of Nuclear Fission*, at one-third the price.

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**Control of the Plant Environment.** Proceedings of the University of Nottingham Easter School in Agricultural Science, 1957. J. P. Hudson, Ed. Academic Press, New York; Butterworths, London, 1957. xvi + 240 pp. \$7.50.

This book is divided essentially into three parts, with discussions by a number of English and Dutch scientists who have carried out work on the control of plant environment. The first part discusses experimental results, especially those concerning effects of temperature and light on a number of plants, such as peanuts, chrysanthemums, irises, lettuce, and grasses. The second part contains an excellent discussion of a number of the factors which have to be taken into account in the construction of controlled environment facilities. The chapter by Morris, particularly, should prove most useful to any designer of plant-growth rooms; it includes an excellent analysis of lighting problems. The third part provides descriptions of installations which are in existence. Particular emphasis is laid on the different installations which are at the moment in existence in England. However, in most cases no performance data are supplied, and it will therefore be difficult for prospective designers to choose from the multitude of types of construction principles.

This book is quite timely because of the enormous recent increase in interest in studies on the effect of environment on performance of plants. These studies can be divided into two distinct groups. In the first place, control of the environment is essential in any careful study of plant behavior. To achieve this control, individual growth chambers are essential, and these have been constructed in fairly large numbers in England, as is seen from this book. In addition, there are problems in ecology, climatology, and especially in the applied botanical fields, where research requires a whole set of controlled environment rooms and greenhouses, covering the complete range of growing conditions, such as a phytotron provides. Several such installations are described briefly in this book, too.

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**The Planet Venus.** Patrick Moore. Macmillan, New York, 1957. 132 pp. Illus. \$3.

As Patrick Moore states in the foreword, his book, *The Planet Venus*, is the first full-length volume ever to be devoted entirely to the general problems of that intriguing planet. In contrast, several score of books have been written

about our other planetary neighbor, Mars.

The reason for this scarcity will be obvious immediately to any reader. Since almost nothing is actually known concerning the physical conditions on the planet and in its atmosphere, the author was able to give adequately, in scarcely 100 pages of text, all of the currently accepted scientific facts and conjectures about Venus, as well as much of the relevant observational and theoretical history.

This work is directed primarily toward the amateur astronomer. The book is very readable, with a distinctly British flavor. The author assumes no previous scientific knowledge on the part of the reader, and hence the material can easily be understood by any person over the age of 15. In addition, the very complete bibliography, fully up to the standard for bibliographies of technical papers in a scientific journal, will be useful to the professional astronomer as well as to the amateur.

Patrick Moore is well qualified to write about Venus. He has been a student of the planet for many years and, since 1955, has directed the Mercury and Venus Section of the British Astronomical Association. Much of the material he presents is necessarily highly conjectural, and the author therefore inevitably injects his personal convictions. Fortunately, he is careful to point out his opinions as such, in cases that might lead to considerable controversy among present-day astronomers. In several other instances his words are so strongly positive that they are unmistakably statements of opinion—although in these cases his opinion is usually shared by all present-day planetary astronomers. For example, on page 62 he writes, "Let us now turn to the celebrated linear streaks or 'canals,' which have been recorded on many occasions but which do not in fact exist at all," and on page 39, "This point of view is obviously unsound. If carried to its logical conclusion, we might well observe Venus with the naked eye and dispense with telescopes altogether!" Nowhere, however, has the author stated opinions with which I basically disagree.

A few minor omissions and errors may be mentioned. On page 60, for instance, the author states that an axial tilt of  $85^{\circ}$  would leave a loophole for shorter rotation periods of about 24 hours, since no Doppler shift could then reveal itself, thus overlooking the fact that even then the earth would at times be above Venus' equator, and that observations could easily be planned to eliminate this possibility. On page 80 he might have referred to the brief history of the earth's atmosphere given on pages 108–109 and on page 113. On page 16 a typographical error ("circle of 'epicycle'" should read "circle or 'epicyc-

cle'") could easily confuse the novice. Reference on page 70 to a nonexistent "frontispiece" is probably also a typographical error; the plate referred to is plate 1, facing page 32.

The book, of course, was written too early to include the recent observations indicating that Venus is a radio source. It does refer to the possibility of radar observations of Venus.

It is perhaps unfortunate that the author included no reference to the extensive literature dealing with observations of the transit of Venus on 9 Dec. 1874. Although, as the author points out, these observations were useless for their intended purpose, they were nevertheless interesting as they related to Venus' atmosphere; for example, the very nicely illustrated book by H. C. Russell, government astronomer of New South Wales, Australia, describes in great detail the effects of the "Cytherean" atmosphere on the Australian transit observations.

On the whole, this book impressed me very favorably. It is a "must" for anyone who wishes to make a serious study of Venus.

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**Strategic Surrender.** The politics of victory and defeat. Paul Kecskemeti. Stanford University Press, Stanford, Calif., 1958. ix + 287 pp. \$5.

This thoughtful book is first of all a study of the Allied policy of unconditional surrender in World War II, but it is more than that. It is a study of the general concept of surrender and of the strategic principles governing it. And it has implications extending beyond the situation that may exist at the end of a total war. It has implications, for example, for what can be expected from negotiations with the Russians in a period of nuclear stalemate.

Kecskemeti, a political analyst with the Rand Corporation, starts by noting that total victory in war can be achieved either by completely overrunning and disrupting the enemy or by his surrender. The enemy, by surrendering when his forces are still intact but when the outcome is no longer in doubt, saves himself and the victor the last painful costs of further fighting. Since the outcome of further fighting is known, the loser cannot hope, by negotiations, to control the terms of surrender. But his residual power to inflict costs on the victor makes it equally a mistake to assume that his bargaining power is nil and to refuse to treat with him. Furthermore, it is often to the victor's advantage to preserve a constituted authority in the enemy territory capable of carrying through the

terms of the surrender rather than to create a vacuum by refusing anything to the loser short of his total collapse.

These conclusions are supported by an analysis of Allied policy of unconditional surrender in World War II. In Italy the Badoglio government was ready to turn the nation's fighting forces against the Germans. The Allies refused to discuss such matters, and confined relations to repeated demands for unconditional surrender—that is, the dissolution of the forces which could have provided some resistance to German occupation. The delays resulting from Allied policy permitted German occupation of Italy, requiring its costly conquest, mile by mile. In Germany the Allied policy made less difference since Hitler, like the Allies, preferred his total military annihilation to negotiated surrender. In Japan the Allies in reality, though not in form, abandoned unconditional surrender, agreeing to the rule of the Emperor to avoid the costs of invasion. Had the Allies been willing to negotiate on this basis earlier, surrender might have followed immediately upon the defeat of Germany, and the use of the A-bomb and Russian entry into the Far Eastern war might have been avoided. These are some of Kecskemeti's points.

The last chapter of the book draws implications for the situation in which each side has power to unleash thermonuclear destruction in desperation on the other, even though this may not avert defeat. The implication is that in such a nuclear stalemate the "political payoffs must be moderate. . . . Imposed terms cannot reasonably be expected to be other than lenient."

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## New Books

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*Actions chimiques et biologiques des radiations*. Les peroxydes organiques en radiobiologie. R. Latarjet. Masson, Paris, 1958. 156 pp. Paper, F. 2800; cloth, F. 3600.

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## Reports

### Some Physical Aspects of the Bacterial Cell

The volume and weight fractions of protoplasm and wall, and the water content, are, in the case of the bacterial cell, interlocking elements of knowledge. When the water content of the cell, and the weight fraction and the volume fraction of either the protoplasm or the wall, are known, the remaining elements can be calculated. The information obtained not only provides additional knowledge concerning the structure of the organism but also tests the self-consistency of experimental results. The information necessary for the calculation has, within the past few years, become available for several organisms.

On the basis of direct isolation procedures, Cooper, Rowley, and Dawson (1) concluded that the cell wall of *Staphylococcus aureus* accounted for 20 percent of the dry weight of the organism. McCarty (2) has reported, also on the basis of direct isolation of cell-wall materials, that the cell walls of group A streptococci make up at least 10 to 15 percent of the dry weight of these cells. More recently, Barkulis and Jones (3) concluded that cell walls make up 23 to 25 percent of the dry weight of group A streptococci. The thickness of the wall of both *S. aureus* and *Streptococcus faecalis* has been estimated by means of the electron microscope to be 150 to 200 Å (4). Electron diffraction studies of group A streptococci (3, 5) suggest that the wall of this organism may be somewhat thicker than that of *Staphylococcus aureus*. Since the electron diffraction studies pertain to desiccated structures in which shrinkage has occurred, the thickness of the walls of the wet cells may be considerably greater than 200 Å. The volume fraction of the protoplasm of cocci

amounts to 0.87 if one uses 4500 Å for the radius of the cell and 200 Å for the thickness of the wall, and 0.81 if one uses 300 Å for the thickness of the wall.

From the data of Weibull (6), the *Bacillus megaterium* cell contains 80 percent water and the volume fraction of the protoplasm amounts to 0.54. Weibull (7) has estimated that the wall of *B. megaterium* represents 20 percent of the dry weight of the cell.

In this report (8) an attempt is made to consider the structural features of the cell which are implied as a consequence of the limitations imposed by the data reported above.

*Assumptions and calculations.* The water content of the cell is an important parameter in the calculations which follow. Group A streptococcal cells, when removed from a water suspension by centrifuging for 15 minutes at 20,000  $\times g$ , yield a tightly packed pellet which, after being lyophilized, has amounted repeatedly to 17 percent of the wet weight (9). The interspace volume for close-packed rigid spheres is 26 percent. If the above interspace volume is taken into account, the water content of the cell becomes 77 percent. In the case of cocci, however, chains of cells are usually present in the culture which would cause the interspace volume of the centrifuged pellet to be greater than 26 percent. When an arbitrarily selected interspace volume correction of 33 percent is applied, the water content of the cell becomes 75 percent. It is apparent that even a considerable error in the correction for interspace volume does not greatly influence a calculation of the water content of the cell.

Mitchell and Moyle (10), employing osmotic methods, found an effective phosphate-impermeable cell volume of 2.42 ml/g of cell dry weight for *Staphylococcus aureus*. If we assume the partial specific volume of the "cell solids" (11) to be 0.72, the water content of *S. aureus*, according to Mitchell's data, becomes 63 percent by weight. The method used by Mitchell, however, may provide the volume of the protoplast rather than that of the whole cell. We have adopted a value of 0.70 as representing a reasonable approximation of the weight fraction of water in the cells of cocci.

The average specific volume of the cel-

lular constituents, other than water, is assumed to be 0.72. The partial specific volumes for most simple proteins, nucleoproteins, and glycoproteins lie between 0.68 and 0.75. The quantity of lipids and dialyzable material (9, 12) represents such a small fraction of the cellular dry weight that the value of 0.72 seems reasonable. Weibull (6) reported a value of 0.70 for the average partial specific volume of the "cell solids" of *Bacillus megaterium*. The factor of electrostriction can be ignored as not seriously affecting density and volume (13).

For simplification the cell is considered to consist of a protoplast surrounded by a wall. It is assumed that the coccus can be represented as a rigid sphere. It seems reasonable to assume, also, that the portion of volume of wall not occupied by "solids" is fully occupied by water.

With volume and weight fractions established, the proportion of water to solids in both wall and protoplast can be readily calculated in terms of an average partial specific volume of the solids.

*Results.* In the case of cocci, the volume fraction of the protoplast has been calculated to be 0.87, as mentioned above. If the relative weight of the cell is taken as 100, and the weight fraction of water in the cell is 0.70, the cell contains 30 weight units of solids. If six weight units—that is, 20 percent—of the solids are in the wall, the relative volume of the cell is

$$30 \times 0.72 + 70 = 91.6.$$

The relative volume of water in the protoplast becomes

$$0.87 \times 91.6 - 24 \times 0.72 = 62.5 \text{ units.}$$

The wall, therefore contains 7.5 weight units of water, and the weight fraction of water in the wall is 0.56. If a weight fraction of water in the cell of 0.75 is used, the fraction of water in the wall is increased to 0.63. It can be seen in Fig. 1 that the thickness of the wall, in the case of cocci, is not especially sensitive to either the radius or the water content of the whole cell. As is shown in Fig. 2 the water content of the wall is, however, for the parameters stated, sharply dependent upon the thickness of the wall. Since the thickness of the wall is related to the structural organization of the solids constituting the wall, the water content probably becomes invariant if the thickness can be established.

In the case of *Bacillus megaterium*, it can be shown that approximately 10 g of water must be present for each gram of "solids" in the wall, for the relationships reported by Weibull (6, 7) to obtain. The protoplasm of this organism, on the other hand, would, according to Weibull's data, contain only 2.5 g of water for each gram of solids. As calculated, the wall of *B. megaterium* contains 91

All technical papers are published in this section. Manuscripts should be typed double-spaced and be submitted in duplicate. In length, they should be limited to the equivalent of 1200 words; this includes the space occupied by illustrative or tabular material, references and notes, and the author(s)' name(s) and affiliation(s). Illustrative material should be limited to one table or one figure. All explanatory notes, including acknowledgments and authorization for publication, and literature references are to be numbered consecutively, keyed into the text proper, and placed at the end of the article under the heading "References and Notes." For fuller details see "Suggestions to Contributors" in *Science* 125, 16 (4 Jan. 1957).

percent water, whereas the water content of the protoplast is only 71 percent. The result seems bizarre. It also follows, on a wet weight basis, that the wall represents 45 percent by weight of the total cell, which agrees with the experimental findings of Weibull (14). The weight fraction of water in the protoplast, 0.71, obtained from the calculation also agrees quite well with that required by the phosphate-impermeable volume found by

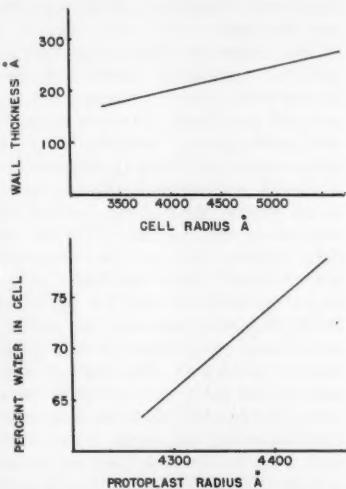


Fig. 1. (Top) Relationship for cocci between the cell radius and thickness of the wall in terms of the parameters listed. Water content of the cell, 0.70; wall dry-weight fraction, 0.20; wall 60 percent water by weight. (Bottom) Relationship for cocci between the radius of the protoplast and the water content of the cell in terms of the parameters listed. Radius of cell, 4500 Å; wall dry weight fraction, 0.20; wall 50 percent water by weight.

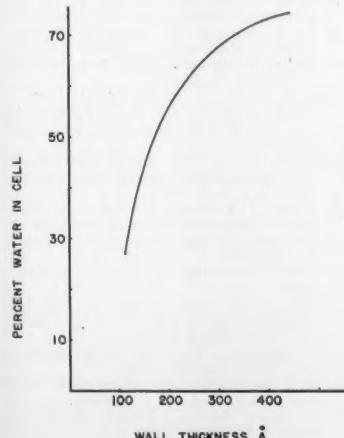


Fig. 2. Thickness of the wall of cocci as a function of water in the wall in terms of the parameters listed. Radius of cell, 4500 Å; wall dry weight fraction, 0.20; weight fraction of water in cell, 0.70.

Weibull (6) to be 2.9 ml/g dry weight. The phosphate-permeable volume accounts for a volume fraction of the cell of 0.54 (6). A volume fraction of 0.54 for the protoplasm is consistent, furthermore, with dimensions for the protoplasm and the cell listed by Weibull (6), for *B. megaterium*.

**Discussion.** In the case of cocci, if all the cellular water and only 50 percent of the cell solids (dry weight) were present in the protoplast and if the protoplasmic constituents were dissolved in the water, the concentration of solids would be greater than 17 percent by weight—a quite unlikely situation. Available evidence indicates that only about 10 percent of the cellular constituents are dialyzable materials of low molecular weight (9, 12). The remaining 90 percent solids (dry weight) appear to be complex proteins and polysaccharides of high molecular weight (9, 12). Few of these substances are likely to be soluble in water to an extent greater than 2 or 3 percent. It seems necessary to conclude that a large fraction of the materials in the protoplast must be present in an undissolved although probably heavily hydrated form. If the weight fraction of the protoplast (dry weight) is substantially greater than 50 percent, the quantity of undissolved matter must increase accordingly.

An alternative possibility would be a protoplast existing as a thick gel. The gel hypothesis has been considered by Mitchell and Moyle (10), and there is evidence against this concept. A third possibility, that the solids present in the wall amount to a much larger weight fraction of the cell than has been reported, should not be ignored.

The above considerations suggest that a quantity of water amounting to more than the weight of the solids is present in the walls of bacteria. In order to accommodate such a quantity of water, the wall could be pictured as a fenestrated three-dimensional network of solid material in which the openings are filled with water. Such a structure would confer the rigidity noted in bacterial walls (15). In addition, the structure would readily permit the physical passage of molecules of some size, which from a metabolic viewpoint is a necessary quality of the wall.

It can be shown by the method indicated above that an increase in the weight fraction of solids in the wall, the volume fraction of protoplasm, or the water content of the cell either independently or in unison, requires an increase in the water content of the protoplasm. Weibull's data are self-consistent in that the calculated water content of the protoplasm agrees well with that found from phosphate-impermeable volume. Other relationships can be found which will provide a protoplasmic water content

agreeing with that obtained from the phosphate-impermeable volume. Such relationships require a decrease in one of the variables when another is increased. For example, if the volume fraction of protoplasm is arbitrarily increased to 0.70, the water content of the cell must be decreased to 0.70 for the protoplasmic water content to remain constant. Under these conditions the wall would still contain 4 g of water for each gram of solids, an amount quite inconsistent however, with experiment (14).

Irrespective of variations in the parameters, the conclusion appears inescapable that the wall of *Bacillus megaterium* contains far more water than solids. Furthermore, the self-consistency of Weibull's data lends credence to their correctness.

In order to account for 10 g of water for each gram of solids in the wall of the cell, an open meshwork in which the wall solids form the structural elements seems a feasible model. In the meshwork the relatively large open spaces could be filled with water. The proposed model is consistent with permeability behavior (6, 10) and electron diffraction studies (16). Bacterial cell walls examined with the electron microscope are relatively transparent (3, 5, 16). An electron micrograph of the wall from *Spirillum* indicates a fenestrated structure with a hexagonal pattern (16).

While it may be coincidental, it is of interest that the thickness of the desiccated wall of *Bacillus megaterium* was found by Piekarski and Giesbrecht (17) to be 150 to 300 Å in thickness, which is approximately one-tenth the thickness observed with wet organisms (6, 18).

The factors considered in this report suggest the usefulness of experimentally determined values for the weight fraction of the dry weight of the cell forming the protoplasm and also for the weight fraction of the total cellular water present in the protoplasm. The present information presents a picture of the bacterial cell as a rigid water-filled mesh inside of which there is a heavy suspension of particulate material. While the concept is not new (10), it was arrived at by reasoning to the best of our knowledge not heretofore applied to microorganisms. The analytical principle utilized is applicable to other bacterial cells and provides a test for self-consistency of assembled physical data.

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## On the Relationship of Serotonin to Schizophrenia

In 1954, Woolley and Shaw (1) formulated the working hypothesis that a cerebral serotonin deficiency or serotonin excess might be a cause of mental disturbances such as those characteristic of schizophrenia. The evidence available at that time which suggested that serotonin played a vital part in the functioning of the central nervous system was of a two-fold nature: (i) serotonin occurs in the

Table 1. Urinary excretion of 5-hydroxyindoleacetic acid in male subjects. S.E., standard error.

Diagnosis	Sub- jects (No.)	Output of 5-HIAA		
		(μg/ml)	(mg/day)	± S.E.
<b>Chronic</b>				
schizo- phrenia*	30†	4.7 ± 0.4	5.3 ± 0.4	
Paranoid	7	4.6	4.3	
Catatonic	3	3.3	5.5	
Hebephrenic	5	3.6	6.2	
Simple	3	6.9	6.2	
Undiffer- entiated	12	4.9	5.4	
<b>Acute</b>				
schizo- phrenia	23†	4.7 ± 0.6	5.5 ± 0.9	
Normal controls	29†	4.4 ± 0.3	5.2 ± 0.3	

\* No. of years hospitalized: median, 9; range, 2 to 27.

† No. of urine collections: chronic schizophrenia, 173; acute schizophrenia, 23; normal controls, 126.

brain, especially in the hypothalamus (2, 3), and (ii) some drugs which act as antimetabolites of serotonin on smooth muscle preparations also cause mental aberrations (4). This is especially true of the powerful psychotomimetic agent lysergic acid diethylamide (LSD). Additional evidence has since been presented by Woolley (5). Further, Sano (6) has reported that the administration of reserpine to psychotic patients causes a temporary increase in urinary 5-hydroxyindoleacetic acid (5-HIAA).

Whether serotonin is involved in the etiology of schizophrenia might be decided by establishing whether serotonin metabolism differs in nonpsychotic well subjects and in schizophrenic patients. We therefore investigated the urinary excretion of its principal metabolite, 5-HIAA, in both groups (7). Untreated male chronic schizophrenic patients (median age, 42 years; range, 24 to 63) were selected from the research wards of the Worcester State Hospital and maintained on the normal hospital diet. Acutely ill male schizophrenic patients (median age, 33 years; range, 16 to 57) were selected from the admission wards, and urine samples were obtained before therapy was instituted. All urine samples were collected in the morning and analyzed by the Udenfriend colorimetric procedure for 5-HIAA (8). The results are shown in Table 1. Statistical analysis shows that there is no significant difference in the excretion of 5-HIAA between chronic or acute schizophrenic patients and nonpsychotic well subjects. These findings agree with those of others (6, 9). The output of 5-HIAA in normal subjects ranged from 0.7 to 13.2 mg/day and in schizophrenic patients from 0.3 to 31.6 mg/day. Bellak (10) has commented on the greater variability of values for almost any factor investigated.

In order to determine the effect of diet on the rate of excretion of 5-HIAA, three normal subjects were maintained for 3 days on each of the following diets with suitable control periods before and between the diets: (i) high carbohydrate, (ii) high fat, (iii) high protein, and (iv) 750 mg/day of L-tryptophan. No unusual effects were found, and all 5-HIAA values were well within the normal range.

In a longitudinal study carried on for 5 weeks, 20 urine samples were collected from each of two chronic schizophrenic patients and from one normal subject, a hospital attendant who ate approximately the same food as the patients. Patient No. 1 excreted an average of 11.0 mg of 5-HIAA per day with a range of 0.7 to 18.9 mg/day. Patient No. 2 excreted 8.6 mg/day with a range of 2.2 to 16.9 mg/day. No correlation between the patients' psychiatric behavior and uri-

nary excretion of 5-HIAA could be demonstrated. The normal subject excreted an average of 5.9 mg/day with a range of 3.1 to 9.8 mg/day.

We also studied the effect of LSD on 5-HIAA excretion in four normal subjects, each of whom received 75 μg of LSD orally. Urine samples were collected immediately before the administration of LSD and 2 hours after. The typical symptoms of the LSD psychosis were evident in less than 2 hours. No significant change in 5-HIAA excretion was observed.

The evidence based on urinary 5-HIAA excretion in chronic and acute schizophrenic patients does not indicate a causal relationship between serotonin and schizophrenia. Preliminary results indicate also that blood serotonin values of chronic schizophrenic patients, measured by the fluorimetric method of Udenfriend and coworkers (11), do not differ significantly from those of normal subjects; the values of both groups ranged between 0.1 and 0.3 μg/ml of blood. However, serotonin metabolism, as measured by serotonin levels in blood and by 5-HIAA in urine, reflects serotonin primarily from the larger body stores. A hypothetical defect in mechanisms involving serotonin would most likely exist in the brain and might not be detectable by the methods employed.

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## Perdeutero Synthetic-Natural Rubber

The recently reported stereospecific polymerization (1) of isoprene and the availability of D<sub>2</sub>O has made possible the preparation of synthetic-natural (SN) rubber in which most of the hydrogen atoms are D atoms.

Acetone-d<sub>6</sub> was prepared (2) from 99.5 percent D<sub>2</sub>O and acetone-h<sub>6</sub> in the presence of K<sub>2</sub>CO<sub>3</sub>. Nine stages were applied. Each required fractionation of acetone from water, and it is estimated that each replaced approximately half of the light hydrogen remaining from the previous stage. Acetylene-d<sub>2</sub> was prepared from D<sub>2</sub>O and calcium carbide. The procedure of Bergmann (3) for the Favorskii (4) reaction of acetylene and acetone to form 2-methyl-3-butyn-2-ol was followed except that in our work perdeutero reactants were used.

The triple bond of the butynol selectively absorbed D<sub>2</sub> over the Lindlar (5) catalyst, and the resulting 2-methyl-3-butyn-2-ol dehydrated readily over Al<sub>2</sub>O<sub>3</sub> to give isoprene-d<sub>8</sub>. Standard fractionation techniques were used for the isoprene and for all the intermediates. The isoprene was finally distilled over sodium to remove acetylenes, acetone, and alcohols. The same methods were applied to the corresponding perprotio derivatives. Table 1 gives the properties of most of the compounds prepared and used in this study.

The isoprene-d<sub>8</sub> polymerization was initiated by TiCl<sub>4</sub> and triisobutyl-h<sub>27</sub>-aluminum in both aliphatic and aromatic solvents. Hydrogen from these solvents did not appear to interchange with deuterium from the monomer or polymer. Isoprene-d<sub>8</sub> polymerizes faster and to a higher molecular weight than isoprene-h<sub>8</sub> under what are believed to be comparable conditions. Our best sample of D-SN rubber was prepared by hexane extraction of a raw polymer containing 25 percent gel. The soluble polymer ( $M_n = 333,000$ ) milled (broke down) like natural rubber and had a limiting intrinsic viscosity in benzene at 25° of  $[\eta]_0 = 5.8$ .

The benzene solutions were found to degrade unless they were stabilized with a small amount of tetramethylthiuram disulfide (TMTD). D rubber evolved (6) a trace of D<sub>2</sub> when it was vulcanized with TMTD and ZnO. The vulcanizate, after removal of zinc compounds and other substances by short-path distillation techniques (7), was nearly transparent and displayed an x-ray diffraction pattern that was superposable over those of natural and SN rubbers. The density at 23°C of the vulcanizate was 1.010 g/ml (equivalent to 1.009 at

Table 1. Properties of perprotio and perdeutero derivatives of compounds and azeotropic mixtures.

Compound or azeotrope	Boiling point (740 mm)	Freezing point	Water (wt. %)	$N_d^{20}$	$d_4^{20}$
<i>Perprotio derivatives of compounds and mixtures</i>					
Acetone	55.3			1.3592	0.7895
Water	99.2	0.0	100	1.3333	0.99823
2-Methyl-3-butyn-2-ol	103	3.0		1.4215	0.8609
2-Methyl-3-butyn-2-ol water azeotrope	89.0	-10.5	27	1.4050	
2-Methyl-3-butyn-2-ol	96.5	-28.0		1.4172	0.8231
2-Methyl-3-butyn-2-ol water azeotrope	85.3	-9.0	23.2	1.4078	
Isoprene	33.3			1.4219	0.6802
<i>Perdeutero derivatives of compounds and mixtures</i>					
Acetone	54.3			1.3565	0.8719
Water	100.6	3.8	100	1.3286	1.1075
2-Methyl-3-butyn-2-ol	102	1.9		1.4188	0.9423
2-Methyl-3-butyn-2-ol water azeotrope	89.5		27	1.4034	
2-Methyl-3-butyn-2-ol	96.0	-28.8		1.4134	0.9185
2-Methyl-3-butyn-2-ol water azeotrope	86.0		20.0	1.4053	
Isoprene	31.8			1.4189	0.7604

25°C); and the density of the polymer before cure was 1.005 g/ml (equivalent to 1.003 at 25°C). Accepting 0.906 g/ml at 25°C as the density of purified natural rubber (8) and multiplying this by the ratio (1.118) of the density of isoprene-d<sub>8</sub> to the density of isoprene-h<sub>8</sub> (see Table 1), we obtain a calculated value of 1.013 g/ml for the density of D rubber. Now the ratio of the formula weight (76.145) of isoprene-d<sub>8</sub> to that (68.119) of isoprene-h<sub>8</sub> is 1.118. It is probable that 0.906 is somewhat high as the density of perprotio all-cis, 1,4, head-to-tail polyisoprene, and values observed for some of our best samples of SN rubber are around 0.901. This, when multiplied by 1.118, gives 1.007 as the expected density of D-SN rubber. The good agreement between the found and expected values of the density shows that our specimen contains at most not more than a few hydrogen atoms.

Study of the boiling points given in Table 1 reveals, except for water where hydrogen-bonding is important, that the perdeutero derivatives boil at lower temperatures than the corresponding perprotio compounds. Assuming boiling point to be a measure of molecular interaction in small molecules and to be of value for predicting segment interaction in a related polymer, it is expected that there would be less polymer-polymer interaction in the case of D rubber than in the case of H rubber. This expectation is confirmed by the interaction coefficient,  $\mu_i$ , found by study of toluene solutions which revealed a value of 0.415 compared with 0.398 for H-SN rubber. It is tempting to predict, therefore, that the dynamic properties of D rubber will be found to be better than those of H rubber.

The infrared spectrum of D-SN rub-

ber is of special interest. For example, it contains a band at 15.20 $\mu$  corresponding to the 11.95- $\mu$  band in H rubber. This finding confirms the previously somewhat doubtful assignment of the 11.95- $\mu$  wavelength to the H atom on the double bond.

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## Succinic Semialdehyde Oxidation by a Soluble Dehydrogenase from Brain

The identification of succinic semialdehyde as a product of transamination of  $\gamma$ -aminobutyrate by brain tissue (1) *in vitro* has led to an investigation of the further metabolism of succinic semialdehyde. Whole homogenates of rat, cat, and monkey brains have been shown to catalyze a diphosphopyridine nucleo-

tide (DPN) dependent oxidation of semialdehydes.

The dehydrogenase has been purified approximately 150-fold from monkey brain to a specific activity of 3  $\mu$ moles/mg of protein per hour at 20°C and pH 8.1, with succinic semialdehyde as substrate. Maximal initial rates are obtained with  $10^{-4}$ M succinic semialdehyde. Triphosphopyridine nucleotide is inactive as a hydrogen acceptor. Aged enzyme preparations require preincubation with cysteine or mercaptoethanol for maximal activity. Glyoxylate and malonic semialdehyde are also oxidized by the preparation, and preliminary experiments indicate that the relative rates with these substrates are species-dependent. 5-Hydroxypentanal is oxidized at a comparatively slow rate, while formaldehyde, acetaldehyde, and glyoxal oxidation was not significant at comparable substrate and enzyme concentrations. A dehydrogenase from *Pseudomonas* exhibiting specificity for succinic semialdehyde is described in an accompanying report (2).

The soluble enzyme from monkey brain was obtained by freezing and thawing the particulate fraction R<sub>s</sub> prepared according to the method of Brody and Bain (3). Further purification was achieved by absorption and elution from nucleic acid and treatment with protamine and Dowex-1 chloride.

The assay system consisted of 1  $\times$   $10^{-4}$ M aldehyde, 4  $\times$   $10^{-4}$ M DPN, 4  $\times$   $10^{-3}$ M mercaptoethanol, and 0.05M tris(hydroxymethyl)aminomethane buffer, at pH 8.1. DPNH formation was measured fluorimetrically in whole homogenates (4) and spectrophotometrically in the case of the soluble enzyme preparations.

Studies with C<sup>14</sup>- $\gamma$ -aminobutyrate have shown that it enters the tricarboxylic cycle rapidly in brain in vivo (5). Although evidence for the importance of other oxidative pathways involving semialdehydes in brain is lacking, the possibility cannot be excluded. Malonic semialdehyde presumably arises from the in vitro transamination of  $\beta$ -alanine (1, 6).

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#### Preparation of Cell Suspensions from Insect Tissues for in vitro Cultivation

Previous studies of the cultivation of insect cells in vitro have followed the classical technique of the explanation of tissues and organs. Insect tissue cultures have been maintained for only relatively short periods of time, and serial passage of the cells has not been achieved. The literature in the field has been reviewed by Schmidt and Williams (1). Much valuable information is presented in recent papers by Grace (2) on culturing techniques, by Loeb and Schneiderman (3) and Loeb (4) on the use of synthetic medium 199 (5), and by Wyatt (6) on the development of a medium based on the chemical composition of silkworm hemolymph. The limited success of these studies with explanted tissue has led us to try another approach to the cultivation of insect cells by modifying the technique of Dulbecco and Vogt (7) to attain a suspension of cells from disaggregated tissue. We wish to report the results of these preliminary studies (8).

The variegated cutworm, *Peridroma marginata* (Haworth) (Lepidoptera: Phalaenidae), is readily available in the San Francisco Bay area and is easily raised in the laboratory. The integument of the thoracic segments of the fifth-instar larva was used for the present study. It is comprised of differentiated larval cells and undifferentiated cells in the wing buds and leucopoietic organs.

Prior to dissection, the larvae were anesthetized for 1 minute in CO<sub>2</sub>. To sterilize the external surface, they were passed successively through 5 percent ethyl alcohol, 4 percent formaldehyde (immersion of the head was avoided), and two changes of 70 percent ethyl alcohol. The excess alcohol was removed on blotting paper, and the dissection was performed in a sterile petri dish with iridectomy scissors. The thoracic segments of five to ten larvae were collected in phosphate buffered saline. They were washed in five changes of the saline to eliminate possible microbial contaminants.

The saline of Dulbecco and Vogt (7) was used, with the following modifications: (i) NaCl 8.0 g, KCl 0.2 g, Na<sub>2</sub>HPO<sub>4</sub> 1.15 g, KH<sub>2</sub>PO<sub>4</sub> 0.2 g, phenylthiourea (twice recrystallized from hot ethyl alcohol) 2.08 g, water (distilled and deionized) 800 ml; (ii) CaCl<sub>2</sub> 0.2 g, MgCl·6H<sub>2</sub>O 0.1 g, phenylthiourea 0.52 g, water 200 ml. The phenylthiourea was included to inhibit the tyrosinase activity in the tissue (1). The two solutions were autoclaved separately and combined when cooled. Prior to use, penicillin (200 units/ml) and streptomycin (100  $\mu$ g/ml) were added.

Disaggregation of the tissue was attempted, initially, with trypsin and Ver-sene, under conditions used routinely in the preparation of vertebrate cell cultures. Although many cells were liberated, they were injured in the process. Cytoplasmic extrusions indicated damage to the cellular membranes which could not be arrested by washing with saline or serum.

Liberation of undamaged cells was accomplished with an extract prepared from the hepatopancreas and crop of the snail *Helix aspersa* Müller. Such an extract is a rich source of hydrolytic enzymes. The snails were starved for 4 to 7 days to empty their digestive tracts of solid materials. The hepatopancreas and crop were removed, their wet weight was determined (0.55 to 1.20 g) and they were immediately ground with an equal weight of distilled water in a Tenbroek tissue grinder, cooled to approximately 4°C. The resultant homogenate was centrifuged at 24,000 g for 15 minutes in a refrigerated centrifuge, and the supernatant was stored in a frozen state at -20°C. Prior to use, the extract was thawed, re-centrifuged, diluted with two volumes of saline, and sterilized by passage through a Millipore filter.

Disaggregation was performed at room temperature in a 50-ml erlenmeyer flask containing the thoracic segments of five larvae and 5 ml of hepatopancreas-crop extract. The contents were stirred gently with a magnetic stirrer. Liberation of the cells was completed in 5 to 7 minutes, as evidenced by the transparency of the larval cuticle and the cloudiness of the suspension. The fluid was pipetted into a centrifuge tube and allowed to stand for 5 minutes to permit the tissue fragments to settle. The cell suspension was decanted into a second tube and centrifuged for 1 minute at 1700 rev/min (clinical centrifuge). The supernatant was discarded, the cells were washed in the saline, and an aliquot was counted in a hemocytometer chamber. The thoracic segments of each larva yielded approximately 160,000 cells. They appeared round and clear, with well-defined nuclear and cytoplasmic membranes.

The cells were re-centrifuged, the saline wash was decanted, and they were suspended in the culture medium. This consisted of medium 199 [modified by increasing the amino acids to the level recommended by Wyatt (6)], 20 percent human serum, and 5 percent chick embryonic extract. Culture tubes were seeded with approximately 400,000 cells in 1 ml of medium and held at room temperature. The cells attached themselves readily to the glass, either singly or in packets of five to ten. They were maintained for 4 to 5 days in a healthy state, flattened, optically clear, and with

normal-appearing nuclei. No effort was made at this time to study the growth requirements of the cells.

This method for preparing cell suspensions from insect tissue is reproducible and makes possible quantitative studies involving large numbers of cells. Conceivably it could provide monolayer cultures for viral research. We are hopeful that the liberated cells may dedifferentiate rapidly and be capable of growth in a less complex medium than is required, apparently, for explanted insect tissues.

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## Protection of Fungi against Polyene Antibiotics by Sterols

While we were studying the structural chemistry of the polyene antifungal agent, filipin, the question arose of the possible mechanisms of its antifungal action (1). The presence of a conjugated polyene structure in filipin suggested that perhaps filipin interfered with the synthesis or the function of carotenoids in the fungi. In order to investigate this hypothesis, a mixture of carotenoids was obtained from carrots. The hexane extract, prepared according to the method of Loomis and Shull (2), was tested by the assay disc method on *Penicillium oxalicum* (3). The inhibitory activity of filipin was, indeed, completely prevented, and the organism grew normally in the presence of filipin plus the crude hexane extract.

Saponification of the hexane extract followed by chromatography on MgO : Hyflo Super Cel gave an active fraction which followed  $\alpha$ - and  $\beta$ -carotene from the column. From this fraction a white material was obtained which was easily crystallized from methanol-water. This material was obviously not the usual type of carotenoid. Moreover, when crystal-

line preparations of  $\alpha$ -carotene,  $\beta$ -carotene, or vitamin A were tested, they showed no activity at levels of 10 times that of filipin. The isolated material melted at 134.5° to 137°C and gave analytical data consistent with a  $C_{20}H_{30}O$  structure. C-Methyl analysis completely ruled out the possibility that this material was a perhydrocarotenoid, for the material contained only 1.5 C-methyl groups per 20 carbons. An alternative possibility that the protecting agent might be a sterol was confirmed by positive Lieberman-Burchard and Salkowski tests. The analytical data are also in good agreement for sterols of the  $C_{29}$  series—that is, sitosterol and stigmasterol (4)—which have been isolated from carrots, if they are calculated for  $\frac{1}{2} H_2O$  of crystallization (5).  $C_{29}H_{30}O \cdot \frac{1}{2} H_2O$ : Calculated: C, 82.18 percent; H, 12.11 percent. Found: C, 82.01 percent; H, 12.46 percent.

The observation that the active agent is a sterol led to the testing of a number of such compounds for similar activity. Thus far, three fungi, *Penicillium oxalicum*, *Aspergillus niger*, and *Hansenula subpelluculosa*, have been used to study this phenomenon. The prevention of filipin inhibition of the *Penicillium* was observed in both the assay plate test and in liquid media. On agar plates, both carrot sterols and soybean sterols allowed growth of *P. oxalicum* to occur in the presence of filipin at a weight ratio of sterol to filipin of 0.5 : 1. *Hansenula* grew normally in shaken liquid culture at a ratio of 0.25 : 1.0. The effect of sterols on nine polyene antibiotics showed various degrees of protection, but no definite relationship between the number of unsaturated groups in the antibiotics and their titration could be established (6). Filipin and fungichromin inhibitions were most readily prevented, followed by amphotericin B, trichomycin, and rimocidin, while candidin A, candidin B, ascosin, and nystatin were only slightly affected. Unfortunately, only the purities of filipin and fungichromin were known so that the relative order of protection can only be tentatively suggested.

Of all the sterols examined thus far, cholesterol, ergosterol, sitosterol, stigmasterol, and to a slight degree, lanosterol, have been active in offsetting filipin inhibition of *H. subpelluculosa*. Ergosterol gives effective reversal of filipin activity; cholesterol is ineffective. None of the short-chain steroids that were tested had similar effects even at a ratio of steroid to filipin of 4 to 1. Apparent reversal occurs after long incubation periods, but preliminary data indicate the possible inactivation of filipin under these conditions.

The prevention of the antifungal activity of filipin by sterols has some interesting implications. Evidently, sterols

play a much more important role in the growth processes of fungi than has hitherto been suspected. While a few microorganisms have been shown to require sterols for growth (7-9), our current studies indicate that such substances are probably essential metabolites for many fungi. This has not been recognized until now because these microbes are for the most part autotrophic for their sterol requirement. Except for *Labryntula vitellina* var. *pacifica* (9) and *Saccharomyces cerevisiae* S C-1 when grown anaerobically (7), the need for this compound has not been demonstrated among the fungi.

The mechanism by which filipin and other polyenes inhibit fungi is intriguing. They might either prevent the synthesis of sterols which are necessary for growth or competitively replace the sterol as a cofactor of a reaction vital to the metabolism of the organism. If the synthesis of cholesterol is prevented, then the inhibition probably occurs at a stage beyond lanosterol formation (10). Squalene does not reverse the action of filipin on *Hansenula subpelluculosa* even at a squalene to filipin ratio of 20 : 1. Lanosterol reverses the antibiotic only very slightly at a lanosterol to filipin ratio of 4 : 1. This is a sharp contrast to cholesterol, which is active at a ratio of under 4 : 1 and probably at  $\frac{1}{4} : 1$ .

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24 March 1958

## Pyrrolidine Metabolism: Soluble $\gamma$ -Aminobutyric Transaminase and Semialdehyde Dehydrogenase

A strain of *Pseudomonas* isolated by the enrichment culture technique with pyrrolidine as the sole carbon source has been found to catalyze the following reactions designated as  $\gamma$ -aminobutyric

Table 1. Activity of  $\gamma$ -aminobutyric transaminase and semialdehyde dehydrogenase (in micromoles per hour per milligram of protein).

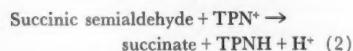
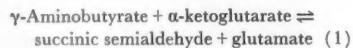
Medium*	Activity	
	Dehydrogenase†	Transaminase‡
Pyrrolidine	1.5	2.3
Aminobutyrate	1.3	1.7
Glucose	0.7	0.1
Glutamate	0	0

\* Carbon source, 0.5 percent plus the following in grams per liter:  $K_2HPO_4$ , 1.5;  $NaH_2PO_4$ , 0.5;  $NH_4NO_3$ , 1;  $MgSO_4 \cdot 7H_2O$ , 0.2.

† Assayed by following the formation of DPNH spectrophotometrically (reaction 2) after the addition of cell-free extract to a system containing the following in micromoles per milliliter: potassium phosphate at pH 7.3, 100; DPN, 1; succinic semialdehyde, 0.2; mercaptoethanol, 5.

‡ Assayed by following the formation of DPNH spectrophotometrically (sum of reactions 1 and 2) after the addition of cell-free extract to a system containing an excess of the dehydrogenase and the following in micromoles per milliliter: potassium phosphate at pH 7.3, 100; DPN, 1;  $\alpha$ -ketoglutarate, 1;  $\gamma$ -aminobutyrate, 1.

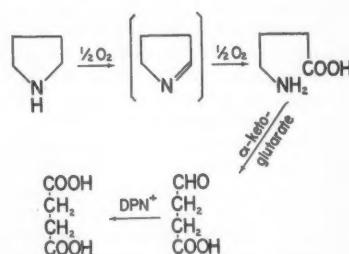
glutamic transaminase (reaction 1) and succinic semialdehyde dehydrogenase (reaction 2):



The transaminase has been separated from the dehydrogenase activity and has been partially purified (85-fold) by protamine treatment, by ammonium sulfate and acetone precipitation, and by absorption and elution from calcium phosphate gel. The reaction appeared to be specific in that  $\beta$ -alanine,  $\Delta$ -aminovaleric acid, or ornithine could not substitute for  $\gamma$ -aminobutyrate in reaction 1; pyruvate, oxalacetate, or  $\alpha$ -ketovalerate could not substitute for  $\alpha$ -ketoglutarate as amino group acceptor. The semialdehyde dehydrogenase (reaction 2) has been separated from the transaminase and has been partially purified (45-fold) by protamine and gel treatment and by ammonium sulfate and acetone precipitation. The reaction is specific for succinic semialdehyde. TPN is eight times as active as DPN at a concentration of 1 mM (1); malonic semialdehyde, glyoxalate, glycolaldehyde, and a variety of aliphatic and aromatic aldehydes were inactive. The reaction has not been experimentally reversed. The best preparations of these enzymes under the assay conditions outlined in Table 1 had specific activities of 4.5 and 3  $\mu\text{mole}/\text{min}$  per milligram of protein for the transaminase and the dehydrogenase, respectively. A particulate preparation from brain had previously been found to catalyze a similar transamination (2). The description of a dehydrogenase from

brain which catalyzes the oxidation of succinic semialdehyde is reported in an accompanying manuscript by Albers and Salvador (3).

That the formation of these enzymes depends on the carbon source employed in the culture medium is shown by the data presented in Table 1. Thus, in the absence of  $\gamma$ -aminobutyrate or pyrrolidine, little transaminase activity could be detected. Similarly, the dehydrogenase content is increased by growth on  $\gamma$ -aminobutyrate or pyrrolidine. Growth did not occur with 2-pyrrolidinone as the carbon source. The simultaneous induction (see 4) of the transaminase and the dehydrogenase when growth occurs on pyrrolidine, as well as the apparently analogous primary degradation of proline (5) and hydroxyproline (6) suggests the following scheme for pyrrolidine catabolism:



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26 February 1958

#### Late Lower Silurian Fossils from Sillimanite Zone near Claremont, New Hampshire

J. B. Thompson has reported the discovery of fossils in the sillimanite zone of regional metamorphism in the extreme western part of Croydon Township, near Claremont, N.H. (1). To the best of our knowledge the Croydon occurrence of generically identifiable fossils in regionally metamorphosed rocks of the sillimanite zone is unique (for a summary of occurrences, see Bucher, 2). The area

has been mapped by C. A. Chapman, and the fossils are in rocks mapped by him as the upper part of the Clough formation (3-5). Detailed remapping by Thompson leads to the same stratigraphic interpretation as that arrived at earlier by Chapman but shows that the fossils are preserved in the nose of a major recumbent fold rather than in a homoclinal sequence as indicated by Chapman's geologic map (4, plate I).

The fossils are preserved as coarsely crystalline calcite in a matrix containing quartz, diopside, grossularite, and hornblende. Argillaceous rocks of the Littleton formation exposed about  $\frac{1}{4}$  mile to the west contain almandite, staurolite, biotite, kyanite, and locally fibrous sillimanite. About  $\frac{1}{8}$  mile to the east, argillaceous rocks of the Littleton formation [mapped as Clough formation by Chapman (4, plate I)] contain almandite, biotite, and sillimanite. The sillimanite is in part in fibrous knots possibly pseudomorphous after kyanite. Some specimens contain staurolite, but it is less abundant than it is to the west. The fossil locality is thus interpreted as lying in the low-grade part of the sillimanite zone.

The fossils occur as a shell bed that has suffered a certain amount of current action, as is indicated by the disarticulated state of the brachiopods. The cardinalia of all the brachiopods are still well preserved, but fine external striae are barely discernible. Study of the fossils by Boucot shows the presence of the following: *Eospirifer* cf. *E. radiatus*, *Plectambonites*, *Resserella* (= *Parmortis*) cf. *R. elegantula*, *Atrypa* cf. *A. reticularis*, *Leptaena* cf. *L. "rhomboidalis*, *Stricklandia* cf. *S. lens ultima*, *Cyrtia* (?), unidentified rostrospiroid brachiopod, unidentified high-spired gastropod, *Porpites* (= *Paleocyclus*) cf. *P. porpita* (6), unidentified zaphrentid tetracorals, *Heliolites*, and *Favosites*.

The presence of a smooth *Stricklandia* lacking outer plates suggests similarity to Williams' *Stricklandia lens ultima* (7, pp. 103-104). Williams records *S. lens ultima* from zones C<sub>4</sub> and C<sub>5</sub> of the Upper Llandovery in the Llandovery region (7, p. 129). The presence of *Porpites porpita* suggests a stratigraphic position near the top of the Upper Llandovery—that is, C<sub>6</sub>—as is indicated by its occurrence in the lower Visby marl of Gotland (Hede, 8) together with a plicated *Stricklandia* (*S. lirata*) and in 7<sub>e</sub> of the Oslo region (9) together with *Stricklandia lirata*. *Porpites porpita* has not been recorded together with fossils of C<sub>4</sub> to C<sub>5</sub> age elsewhere, whereas uniplated or sparsely plicated species of *Stricklandia* do not occur elsewhere as high as C<sub>6</sub> or its equivalent. *Porpites porpita* is known in New York from the Upper Clinton Schroeppel shale (10, p. 350) and in

Pennsylvania from the uppermost Rose Hill shale (zone of *Mastigobolina typus*) of upper Clinton age (11, p. 362). It is concluded that the upper Clough formation of Croydon Township is of C<sub>5</sub> to C<sub>6</sub> (= Upper Clinton) age, but that, pending further information regarding the lower range of *Porrites porpita* and the upper range of unplaced species of *Sticklandia*, it is not possible to arrive at a more definite conclusion regarding its age.

The Croydon Township occurrence of uppermost Lower Silurian strata containing marine fossils provides an eastern limit for the nonmarine sedimentation of Clinton age in eastern New York, plus adjacent parts of New Jersey and Pennsylvania. In New York the transition from marine to nonmarine strata of Clinton age takes place near Utica (10, pp. 339-340) and south-southwestward in Pennsylvania (12, Fig. 2) near the Delaware Water Gap. Therefore, the maximum width of the region formerly occupied by nonmarine, late Lower Silurian strata is about 140 miles.

Strata of Silurian age (13) occur near Bernardston, Mass., in what appears on a lithologic basis to be the same stratigraphic position as the Croydon occurrence. A stratigraphic sequence similar to that occurring in the Croydon area appears to extend south through central Massachusetts (14, plate X) and into Connecticut (15).

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24 March 1958

15 AUGUST 1958

## Adaptation of Tissue Culture Cells to a Serum-Free Medium

Many attempts have been made to develop simplified tissue-culture media. The main difficulty encountered has been replacement of the serum component. Recent developments include media which contain various additives or serum fractions in addition to a basal constituent (1) and those directed toward a medium which is chemically defined (2). This paper reports the adaptation of a line of mouse lung cells to a serum-free medium.

The mouse lung cells used in this work were isolated from lung tissue of newborn Swiss mice (NIH strain). The usual trypsinization methods were used for isolation. Prior to adaptation, the cells were in their 110th passage on a medium consisting of 10 percent horse serum and 90 percent medium 199 (3). Penicillin and streptomycin were each added in a concentration of 50 units per milliliter. Morphologically, the cells appeared fibroblast-like, although small numbers of epithelioid cells were in evidence. These cells were routinely passed every 4 days by trypsinizing, washing, and inoculating (hemocytometer count) approximately  $3 \times 10^6$  cells/ml in T-30 flasks, the total medium volume being 5 ml.

The medium which proved best for adaptation consisted of 99 percent medium 199, 1 percent Difco Bacto Peptone, 100 mg percent glucose, and the usual 50 units each of penicillin and streptomycin per milliliter. The cells passed on this medium were removed from the glass surface by scraping with a bent glass rod and were further separated by repeated pipetting. They were inoculated into T-30 flasks at a concentration of  $6 \times 10^6$  cells per milliliter. If trypsin was used to remove the cells, no growth occurred on the serum-free medium. The fact that growth occurs on serum-containing media when this enzyme is used is probably due to the "detoxifying effect" of the serum on the trypsin carried over with the cells.

Growth of the first four passages on the Bacto Peptone medium was slow, requiring several weeks before the bottom of the flask was covered. Subsequent growth was more rapid, allowing transfers to be made every week. At the present time the cells are in their 27th serum-free passage and are being passed every 4 days at a concentration of  $4 \times 10^6$  cells per milliliter. Primary-growth studies indicate that there is a three-fold increase in cells in 4 days. Aliquots of various passages passed on medium 199 plus 100 mg percent glucose without Bacto Peptone have failed to show a demonstrable increase in cell number and routinely do not survive more than three or four passages.

Attempts to adapt human liver and

HeLa cells to this type of medium have failed, but a line of cells isolated from guinea pig lung tissue has survived early passage and may adapt.

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## Transmission of *Pasteurella tularensis* among Desert Rodents through Infective Carcasses

Although Ussov in 1937 (1) mentioned the "phenomenon of carnivores" as being important in the propagation of tularemia epizootics, a review of available literature reveals no supporting experimental evidence. However, Quan in 1954 (2) demonstrated oral transmission of *Pasteurella tularensis* to laboratory animals by feeding on infective flesh. Also, in a preliminary experiment conducted by one of us (E. D. V.), it was found that five species of desert rodents contracted tularemia by feeding on the infective flesh of native deer mice (3). The present study was conducted in an attempt to determine the extent to which desert rodents may feed on animal matter and the potential importance of ingestion of infective flesh as a means of transmission of tularemia among desert rodent populations (4).

Eleven species of rodents native to the Great Salt Lake Desert in Utah were used in this experiment (Table 1). The deer mice and grasshopper mice were laboratory-reared; the other species were live-trapped in the field and held in quarantine for a minimum of 30 days before use. During the course of the experiment, each animal was maintained in a separate cage.

The Schu A strain (5) of *P. tularensis* cultured in a modified casein partial hydrolyzate liquid medium (6) was selected as the infectious agent. The LD<sub>100</sub> for deer mice was determined to be 1 to 10 organisms.

Healthy deer mice inoculated intraperitoneally with approximately 1000 organisms were held until they were moribund or dead of tularemia. A moribund or dead deer mouse was then

Table 1. Tularemia in rodents after ingestion of infective carcasses. All fed animals became infected.

Species	Common name	No. used	No. fed	Day of death or sacrifice
<i>Onychomys leucogaster</i>	Northern grasshopper mouse	16	16	3-4
<i>Citellus leucurus</i>	Antelope ground squirrel	16	15	3-4
<i>Eutamias minimus</i>	Least chipmunk	6	5	3-7
<i>Reithrodontomys megalotis</i>	Western harvest mouse	8	5	3-6
<i>Peromyscus maniculatus</i>	Deer mouse	16	13	3-5
<i>Peromyscus crinitus</i>	Canyon mouse	15	10	3-4
<i>Peromyscus truei</i>	Pinyon mouse	16	15	3-6
* <i>Dipodomys microps</i>	Chisel-toothed kangaroo rat	16	15	3-6
* <i>Dipodomys ordii</i>	Ord kangaroo rat	16	11	3-7
* <i>Neotoma lepida</i>	Desert wood rat	16	10	4-7
* <i>Perognathus parvus</i>	Great Basin pocket mouse	16	4	5-6

\* Required starvation periods of 48 hours before carcasses were introduced.

placed with each of the experimental animals, from which food and water had been withheld for 24 or 48 hours. At the end of 24 hours the carcasses or remains were removed, and food and water were restored to the test animals.

When the exposed animals died, or when they exhibited acute symptoms of infection, they were autopsied, or killed and autopsied, and liver and spleen homogenates were cultured on glucose cysteine blood agar. If *P. tularensis* was not isolated by culture, 0.2-ml aliquots of the liver and spleen homogenates which had been kept frozen at -28°C were inoculated intraperitoneally into healthy deer mice in a further attempt to isolate the organism. Those animals that survived exposure to infective carcasses were held for 14 days, after which they were killed and autopsied. The tissues were examined for *P. tularensis* as outlined above. In all cases definitive identification of the isolated organisms was made by specific slide agglutination tests.

Under the experimental conditions described, the first seven species listed in Table 1 showed little reluctance to feed on deer mouse carcasses. Most of the ground squirrels and chipmunks readily consumed the entire carcass, while the other rodents generally ate only the anterior part of each carcass. The pocket mice, wood rats, and kangaroo rats were reluctant to eat the dead flesh unless regular food supplies were withheld for 48 hours.

In all cases, every rodent that ingested infective flesh contracted tularemia; those that did not ingest infective flesh did not contract the disease.

Although the extent to which wild rodents supplement their natural diet with flesh has not yet been determined, these results indicate that carnivorous among desert rodents may occur and that it may be of importance not only in the maintenance of this disease in nature,

but also in the propagation of tularemia epizootics. The first seven species listed in Table 1 must be considered to be potentially capable of contributing to the maintenance and dissemination of tularemia among desert rodent populations. Because of their reluctance to feed on dead flesh, the other four species must be considered of somewhat less importance in the transmission of this disease.

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29 April 1957

#### Radio-frequency Resistive Impedance Pulsations over the Heart, Lungs, and Abdomen

The accurate timing of the major volumetric events in the atria, ventricles, lungs, and periphery of the human body may easily be accomplished without blood letting by surface study of the electrical resistive impedance changes around or over a given region of the human subject. Figure 1 illustrates the relative amplitude and direction of the pulsatile vertical impedance changes observed during held respiration over a 5 by 5 cm ventral surface area. These changes were studied in progressive areas

in the left mid-clavicular line downward from the clavicle to the region below the umbilicus. Pertinent landmarks in the transition are identified together with the distance in centimeters below or above the sternal angle of our normal adult male subject. Control electrocardiogram and deltoid-chest-deltoid tetrapolar electrical resistive impedance plethysmogram (1-4) serve to line up the corresponding tracings from each level. A decrease in electrical resistive impedance records upward in the trace and corresponds to an increase in volume pulsations. The paper speed is 50 mm/sec.

The study shows that with constant instrumental sensitivities the largest segmental impedance pulsations are found directly over the heart and apical regions 10 to 15 cm below the level of the sternal angle. The minimal impedance pulsations occur in the abdomen at the level of the umbilicus or lower.

An increasing volume pulse is present above the sternal angle and corresponds in its systolic upstroke with the control impedance systolic pulse of the upper torso body segment. These events begin about 0.11 to 0.12 second after the onset of the ventricular QRS of the electrocardiogram. These result from expansion of the great vessels, lungs, and chest segments with blood.

Just below the sternal angle level, we observe a transitional resistive impedance curve having a sigmoid-shaped downward deflection beginning 0.02 to 0.04 second after the onset of QRS in the electrocardiogram and 0.08 to 0.10 second before the control impedance pulse. This event is probably due to contraction of the atrial blood pool, which produces a decreased electrical conductance. A similar early change occurs at -10 and -15 cm below the sternal angle.

The initial ventricular emptying is best seen at -10 and -15 cm (reduced to 1/5 scale) in this case. Like the atrial tracing, it is also directed downward in the record. It is also sigmoid in shape and begins simultaneously with the positive pulse in the control tracing at 0.10 to 0.12 second after the onset of QRS deflection. The ventricular refilling at the -15-cm segment corresponds to the completion of the T wave of the electrocardiogram at 0.36 second after the onset of QRS deflection. A distinct notching or inflection occurs simultaneously with the onset of the U wave of the electrocardiogram in the record at 0.40 second. Since we did not take a simultaneous phonocardiogram, we cannot ascertain in this study whether it is signaled by dynamic events in the heart valves.

Figure 2 illustrates our observations, in the same subject, of resistive imped-

ance pulsations in a transverse line across the chest at the level of the heart. Controls and sensitivities are the same as those in Fig. 1. The traces in the upper line are identified in five 5-by-5-cm positions over the right and left chest and precordium. The dominant systolic positive pulsations over the right and left axillary lines are probably derived from the systolic arrival and distribution of blood to the lungs and underlying chest wall. The rising systolic slope begins simultaneously with the control upper chest pulse at 0.10 second after the onset

of QRS deflections, and it extends beyond the end of the T wave of the electrocardiogram. Compared with the control pulsation, it appears to be an overly damped volume pulse. Both pulsations are produced by the movement of blood away from the heart before the diastolic event which follows the closure of the pulmonic valve.

The evidence by electrical resistive impedance for atrial contraction is observed in the records immediately to the right of the mid-sternum, 0 to 5 cm to the left of the mid-sternal line, and most

marked in the 5- to 10-cm segment from the mid-sternal line over the heart region. As in Fig. 1, the early onset of a decreasing blood pool begins about 0.02 to 0.04 second after the onset of QRS deflection. On the basis of simultaneous pressure studies in the pulmonary artery, brachial artery, and right ventricle, we believe that this event precedes the ventricular contraction and that it is probably related to auricular contraction. Additional evidence for this has been obtained and suggested by the close correspondence of the roentgenophotokymograms of the right and left auricular areas of another subject. The time interval between the impedance event over the atrial region and the subsequent positive pulsation in the upper chest is only 0.06 second. It appears, therefore, that some of the atrial contraction may have escaped detection except as a positive event since the P-R interval of the electrocardiogram in this case measures 0.12 to 0.14 second. In a case of auricular fibrillation, the atrial impedance deflection was absent, and the major pre-cordial systolic impedance change corresponds to the systolic phase of increasing right intraventricular pressure. An isometric ventricular contraction effect in the impedance pulse is often distinct and proven in cases of atrial fibrillation with simultaneous intraventricular and direct pulmonary artery pressures.

In conclusion, electrical resistive impedance measurement of the chest and precordium reveals changes characteristic of atrial, ventricular, lung, and great vessel volume pulsations. The influence of stream line flow during the cardiac cycle may be a factor in the pulsatile change but cannot be dissociated from the major volume change. The dynamic cardiac and vascular events are easily recorded for long intervals without discomfort to the subject (2).

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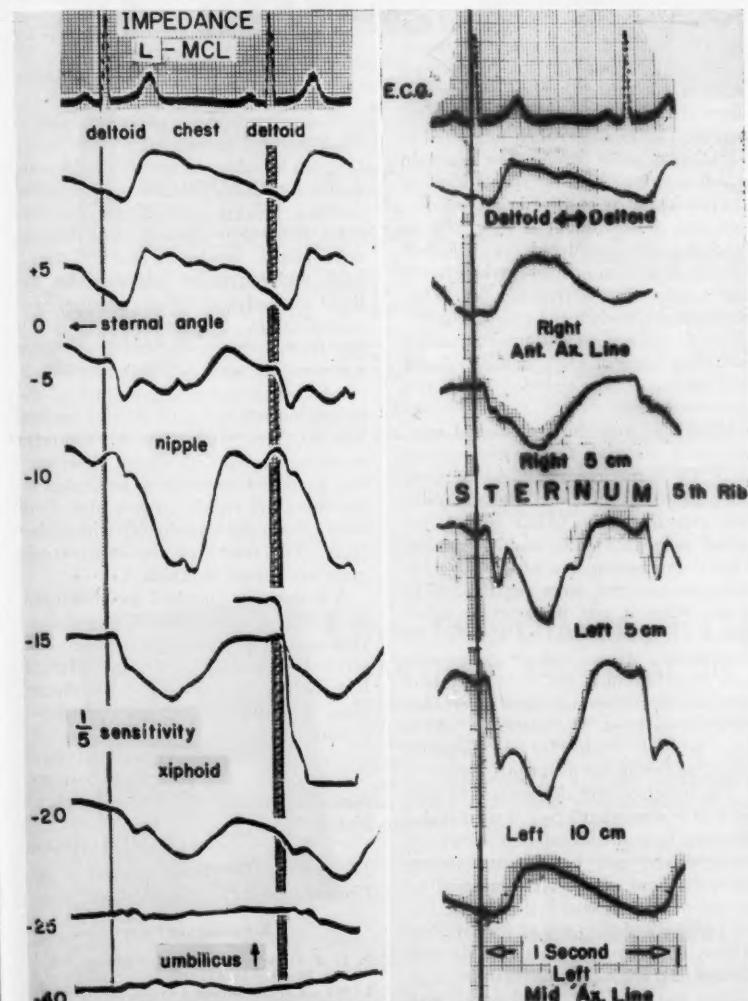


Fig. 1. (Left) Comparison of impedance pulsations between shoulders, and over 5-cm areas in left mid-clavicular line of chest and abdomen simultaneously with electrocardiogram (upper graph). The numerals indicate distance above or below level of sternal angle. The thin vertical line corresponds to the beginning of the QRS complex. Fig. 2. (Right) Comparison of impedance pulsations of 5-by-5-cm areas selected over the anterior chest from the right to left anterior axillary line at about the level of the fifth rib at the sternum. The shoulder-to-shoulder pulse and the electrocardiogram were recorded simultaneously with each study and then were lined up to correspond with the beginning of QRS complex in the graph.

#### References and Notes

1. J. Nyboer, S. Bagno, A. Barnett, R. H. Halsey, *J. Clin. Invest.* 19, 963 (1940); J. Nyboer, *Medical Physics* (Year Book Publishers, Chicago, Ill., 1950), vol. 2, p. 736; F. H. Bonjer, *Circulatieonderzoek door Impedantiemeting* (Oppenheim, Groningen, Netherlands, 1950); J. Nyboer, *IRE Trans. Med. Electronics PGME-3* (1955), p. 5.
2. This project was supported in part by grants from the American and Michigan Heart Associations, Parke Davis and Co., and A. J. Meyers Pharmacy. Dr. Harper Hellens, of Harper Hospital, and Dr. Richard V. Judge, of the Veterans Administration Hospital, Ann Arbor, Mich., were associated in this study. We are grateful to Mr. William Heston for technical assistance.

5 February 1958

## Detection of Hog Cholera Virus by Its Effect on Newcastle Disease Virus in Swine Tissue Culture

Investigations of hog cholera virus (HCV) have been hampered by the lack of laboratory hosts more convenient than swine. In view of the recent widespread application of tissue-culture technique for virus studies, our efforts to discover such hosts have been concentrated on this technique. Hog cholera virus has been known to multiply in swine tissue culture, but the tissue-culture technique has achieved only limited application for HCV studies because the cytopathogenic changes produced are discernible only by elaborate observation (1). In order to discover simple means to determine HCV infection in swine tissue culture, we studied the interaction between HCV and other viruses in this system and found an exalting effect of HCV on Newcastle disease virus (NDV). This effect has subsequently proved to be usable for detection of HCV. This method, designated the END method (Exaltation of NDV), was successfully applied for detecting and measuring HCV and its neutralizing antibodies.

The principle of the method is based on the following findings: (i) Hog cholera virus proliferates in swine testicle cell monolayer culture without any cytopathogenic effect discernible by low-power microscopy. (ii) Under certain experimental conditions (see below), NDV (Miyadera strain) shows little or limited multiplication without any cytopathogenic effect when it is inoculated into the culture within 5 days of cultivation, whereas NDV multiplies well with cytopathogenic effect when it is inoculated into the same culture after 6 to 8 days of cultivation. (iii) In the culture which receives HCV in the initial stage of cultivation, NDV readily proliferates with marked cytopathogenic effect even if it is inoculated as early as the third or fourth day of cell cultivation.

In order to obtain a clear-cut difference in response to NDV between HCV-infected and control cultures, the experimental conditions must be carefully adjusted. In particular, the bovine serum in the culture medium should be carefully selected, because only 4 of 20 sera hitherto tested have been found to be suitable for this purpose, while the remaining sera produced more or less cytopathogenic effect in control as well as in HCV-infected cultures, or only in-

complete cytopathogenic effect in HCV-infected culture after NDV infection.

Careful studies of the various factors involved in the phenomenon finally resulted in the following standard procedure: Testicles aseptically removed from piglets weighing about 15 kg are trypsinized, and a 7 percent cell suspension is made in culture medium (10 percent bovine serum and 0.5 percent lactalbumin hydrolyzate in Hanks' balanced salt solution), and distributed in 11- by 150-mm tubes in 0.9-ml amounts; 0.1 ml of HCV material is then added to each tube, and the tubes are then incubated at 37°C in a slanted, stationary position. The medium is changed on the third day. On the fourth day the tubes are inoculated with about  $10^6$  plaque-forming units of NDV in 1.0 ml of culture medium after culture medium has been removed. The tubes are then incubated at 37°C in a roller drum. The tubes in which a cytopathogenic effect develops are considered as positive in HCV infection and those without development in 3 days are considered as negative. Hemagglutination of fowl erythrocytes is also employed as a criterion, for it becomes positive when the cytopathogenic effect develops. Cell cultures inoculated with either one of HCV and NDV and with no viruses are included in the test as controls.

Using this procedure, we tested various swine materials for the presence of HCV. Of 28 specimens of bloods, serums, and organ tissues obtained from naturally and experimentally (ALD strain) infected swine, 23 gave positive results, while the remaining five, supposedly with low virus contents, were negative. ALD strain, when it was passaged in swine spleen (11 generations) or testicle (25 generations) tissue culture invariably gave positive results. All of 38 specimens obtained from normal swine were invariably negative. The materials which gave positive results became negative after irradiation by ultraviolet light.

The infective titer determined by this method is somewhat lower than that determined by swine inoculation. However, its sensitivity can be enhanced when serial dilutions of the virus material to be tested are first enriched in swine tissue culture and then tested for virus by this method (two-step method). In one of such tests the titer (spleen roller tube culture was used for enrichment) was 0.1 ml of  $10^{-6}$ , while the titer obtained without enrichment was 0.1 ml of  $10^{-3}$ .

Table 1. Titration by the END method of neutralizing antibodies produced in two swine which received crystal violet vaccine (5 ml for swine No. 50, 50 ml for swine No. 51) and, 3 weeks later, active HCV (ALD strain, 10,000 mld).

Vac- cine	Active virus	Weeks after		Titer*
		No. 50	No. 51	
0		0	0	
3	0	1:2	1:8	
4	1	1:1024	1:2048	
5	2	1:1024	1:1024	

\* Serum dilution against 8 ID<sub>50</sub>'s determined by the END method.

and that for subcutaneous inoculation into swine 1.0 ml of  $10^{-5}$ .

The cytopathogenic effect occurring in HCV-infected culture after NDV infection can be inhibited specifically by anti-serum for HCV. One volume of serum dilution (heated at 56°C for 30 minutes) and one volume of virus dilution were mixed, incubated at 37°C for 1 hour, and tested for infectivity by the END method with 0.1-ml amounts. No neutralization was shown with 20 or 21 sera from normal swine purchased from a nonenzootic area, while the remaining one had neutralizing activity in 1:2 dilution, but not in 1:10 dilution against 100 ID<sub>50</sub>'s of HCV. On the contrary, swine vaccinated with crystal violet vaccine produced neutralizing antibodies in low titers and rapidly in very high titers after subsequent injection(s) with active HCV. The results of one such experiment are shown in Table 1.

A new *in vitro* method was developed for detecting and measuring hog cholera virus and its neutralizing antibodies. The method is based on the exalting effect of hog cholera virus on Newcastle disease virus in swine testicle cell monolayer culture (2).

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University of Tokyo

### References and Notes

1. D. P. Gustafson and C. M. Pomerat, *Am. J. Vet. Research* 18, 473 (1957).
2. We are greatly indebted to Dr. S. Ishii of the National Institute of Animal Health for his helpful suggestions.

17 March 1958



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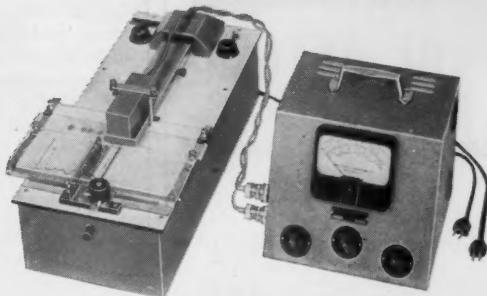
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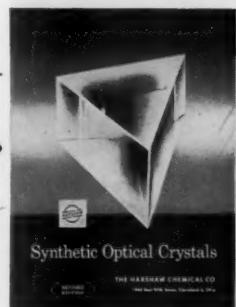
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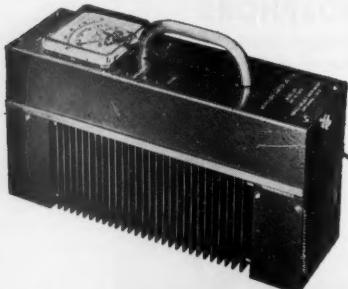
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## Meetings

### Study of Human Biology

Although there are many scientific societies for the furtherance of the biological study of man as an individual, there has been no organization in Great Britain catering to those (such as physical anthropologists or human geneticists) concerned with human populations. The need for such an association was made clear at an informal symposium held at the Ciba Foundation in November, 1957, when papers were given on "The scope of physical anthropology and human population biology and their place in academic studies." Such a society was founded on 7 May 1958 at the British Museum (Natural History) and was named the Society for the Study of Human Biology. Its aims are to advance the study of the biology of human populations and of man as a species, in all its aspects, particularly those of human variability, genetics, ecology, adaptability, and evolution. This it will do, not only by organizing scientific meetings, for proffered papers, and symposia, but also by ensuring a continuity of workers for long-term research projects in the field.

The elected members of the committee for 1958-59 are as follows: Chairman, A. C. Stevenson (director, M.R.C. Unit for Human Genetics, Oxford); vice chairman, J. Z. Young (department of anatomy, University College, London); general secretary, J. S. Weiner (department of human anatomy, Oxford); programme secretary, G. Ainsworth Harrison (department of anatomy, Liverpool); treasurer, E. H. Ashton (department of anatomy, Birmingham); committee members: N. A. Barnicot (anthropology department, University College, London), M. J. R. Healy (Rothamsted Experimental Station, Harpenden), A. E. Mourant (Lister Institute, London), J. R. Napier (department of anatomy, Royal Free Hospital, London), K. P. Oakley [British Museum (Natural History)], and J. M. Tanner (Institute of Child Health, London).

After the meeting, members were shown some of the work in progress in the anthropology section of the British Museum. The original Rhodesian (Broken Hill), Gibraltar I and II, and Singa skulls were available for inspection. Selected recent skulls and jaws showing abnormalities of genetical interest were examined and discussed. The anthropological library and the store of skeletal material and associated laboratories were visited. As an example of the cast-making undertaken here, members were shown casts of the hand bones of *Proconsul* (to be described by Napier and Davis in a forthcoming monograph).

In the paleontological laboratory, the use of radiometric assay in the relative dating of fossil bones was demonstrated. In the serological laboratory, Madeleine Smith described the research she has begun on the blood typing of bones, aimed mainly at improving the available techniques and defining the limits within which they can be reliably applied to ancient material.

J. S. WEINER

*Anthropology Laboratory,  
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Oxford University, Oxford, England*

G. A. HARRISON

*Anthropology Laboratory,  
Department of Anatomy,  
University of Liverpool,  
Liverpool, England*

### Geological Conference

Copies of the first circular for the 21st International Geological Congress may be obtained upon request from the American Geological Institute, 2101 Constitution Ave., NW, Washington 25, D.C. All persons who request the first circular will be placed on the mailing list to receive travel literature and other pertinent information.

### Leprosy

The 7th International Congress of Leprosy, originally scheduled for India, will be held in Tokyo, Japan, 12-19 November 1958. The sponsoring organizations are the International Leprosy Association, the Japanese Leprosy Association, and the Tofu Kyo-kai (Japanese Leprosy Foundation).

### Forthcoming Events

#### September

15-18. American Rocket Society, national, Detroit, Mich. (A. F. Denham, 925 Book Bldg., Detroit 26.)

14-19. Instrument-Automation Conf., 13th annual, Philadelphia, Pa. (H. S. Kindler, Instrument Soc. of America, 313 Sixth Ave., Pittsburgh 22, Pa.)

15-20. Agriculture, European Confederation, Vienna, Austria. (European Confederation of Agriculture, Pestalozzi-strasse 1, Brugg, Argovie, Switzerland.)

15-20. Carboniferous Stratigraphy and Geology, 4th intern. cong., Heerlen, Netherlands. (Secretary, 4th Carboniferous Cong., Geological Bureau, Akerstraat 86-88, Heerlen.)

16-20. Nuclear Electronics, Intern. symp., Paris, France. (Colloque Electronique Nucléaire, 10, avenue Pierre-Larousse, Malakoff (Seine), France.)

16-24. Glaciär Movement Symp., Chamonix, France. (International Assoc. of Scientific Hydrology, 61, rue de Ronces, Gentrugge, Belgium.)

21-25. Differential Anthropology, 5th intern. cong., Amsterdam, Netherlands.

(R. A. M. Bergman, Royal Tropical Inst., Linnaeusstraat 2A, Amsterdam.)

21-28. Poultry Science, 11th world cong., Mexico, D.C., Mexico. (E. Karpoff, Agricultural Marketing Service, USDA, Washington 25.)

22-24. Standards Engineers Soc., 7th annual, Philadelphia, Pa. (Standards Engineers Soc., Box 281, Camden 1, N.J.)

22-25. Scientific Instruments of the 16th to the 19th Century, symp., Frankfurt/Main, Germany. (International Union for the History and Philosophy of Science, 4, rue Thenard, Paris 5<sup>e</sup>, France.)

22-27. High-Speed Photography, 4th Intern. cong., Cologne, Germany. (Royal Photographic Soc., 16 Princes Gate, London, S.W.7, England.)

23-25. Fat Research, 3rd Intern. cong., Seville, Spain. (J. M. Martinez, Instituto de la Grasa, Avenida de Heliopolis, Seville.)

23-30. Rheology, 3rd intern. cong., Bad Oeynhausen, Germany. (R. S. Marvin, Rheology Section, Natl. Bureau of Standards, Washington 25.)

24-26. Mass Spectrometry Meeting, London, England. (R. A. Friedel, U.S. Bureau of Mines, 4800 Forbes St., Pittsburgh 13, Pa.)

24-28. Angiology and Histopathology, 3rd intern. cong., Venice, Italy. (L. Gerzon, Intern. Committee on Angiology and Histopathology, 4, rue Pasquier, Paris, France.)

26-6. International Council of Scientific Unions, 8th general assembly, Washington, D.C. (W. W. Atwood, Natl. Research Council-Natl. Acad. of Sciences, Washington, D.C.)

28-2. Electrochemical Soc., semiannual, Ottawa, Ontario, Canada. (R. K. Shannon, 1860 Broadway, New York 23.)

29-1. Analytical Chemistry in Nuclear Reactor Technology, 2nd conf., Gatlinburg, Tenn. (C. D. Susano, Oak Ridge Natl. Lab., P.O. Box Y, Oak Ridge, Tenn.)

#### October

1-8. Speleology, 2nd intern. cong., Bari, Lecce, and Salerno, Italy. (F. Anelli, Castellana-Grotte (Bari), Italy.)

2-5. International Soc. of Audiology, 4th cong., Padua, Italy. (M. Arslan, 37, via Altinate, Padua.)

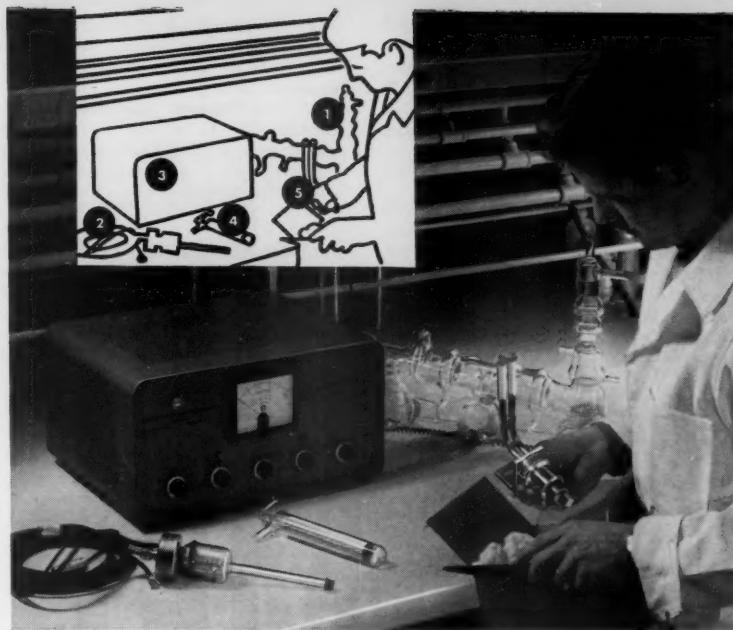
2-6. International Soc. of Scientific Unions, 8th general assembly, Washington, D.C. (W. Atwood, Natl. Research Council-Natl. Acad. of Sciences, 2101 Constitution Ave., NW, Washington 25.)

4-8. Hydrology and Climatology, intern. cong., Lacco Ameno and Ischia, Italy. (Segreteria del Comitato Organizzatore, Congresso Internazionale di Idrologia e Climatologia, Viale Castrense, 9, Roma, Italia.)

4-13. International Federation of Agricultural Producers, 10th conf., Brussels, Belgium. (IFAP, 1624 Eye St., NW, Washington, D.C.)

5-8. American Inst. of Mining, Metallurgical, and Petroleum Engineers, fall, Houston, Tex. (E. O. Kirkendall, AIME, 29 W. 39 St., New York 18.)

6-11. Electroencephalographic Study of the Higher Nervous Activity Processes in Animals and Man, colloquium (by invitation), Moscow, U.S.S.R. (Miss Mary A. B. Brazier, Massachusetts Neurophysiologist)



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logical Laboratory, Massachusetts General Hospital, Boston 14.)

7-9. International Soc. for the History of Pharmacy, cong., Venice, Italy. (A. F. Vitolo, Piazza Carrara 10, Pisa, Italy.)

8-12. Nutrition and Vital Substances, 4th intern. conv., Essen, Germany (Secretary General, Bemeroder Strasse 61, Hannover-Kirchrode, Germany.)

11-15. Salinity Problems in the Arid Zones, UNESCO symp., Tehran, Iran. (UNESCO, 19, avenue Kleber, Paris 16<sup>e</sup>, France.)

12-17. American Acad. of Ophthalmology and Otolaryngology, Chicago, Ill. (W. L. Benedict, 100 First Ave. Bldg., Rochester, Minn.)

13-15. Association of American Medical Colleges, 69th annual, Philadelphia, Pa. (W. Darley, AAMC, 2530 Ridge Ave., Evanston, Ill.)

13-15. National Electronics Conf., Chicago, Ill. (L. W. Von Tersch, Michigan State Univ., East Lansing.)

13-16. Society of Exploration Geophysicists, 28th annual intern., San Antonio, Tex. (C. C. Campbell, Box 1536, Tulsa 1, Okla.)

13-17. American Soc. of Civil Engineers, annual conv., New York, N.Y. (W. H. Wisely, ASCE, 33 West 39 St., New York 18.)

19-22. Land and water, Soil Conservation Soc. of America, 13th annual,

Asheville, N.C. (H. W. Pritchard, executive secretary, 838 5th ave., Des Moines 14 Iowa.)

19-24. American Soc. of Anesthesiologists, Pittsburgh, Pa. (J. E. Remlinger, 802 Ashland Ave., Wilmette, Ill.)

19-26. Allergology, 3rd intern. cong., Paris, France. (S. M. Feinberg, Medical School, Ward Memorial Building, 303 East Chicago Ave., Chicago, Ill.)

19-26. Medical Hydrology, 21st intern. cong., Madrid, Spain. (Dr. Francon, 55, rue des Mathurins, Paris 8<sup>e</sup>, France.)

20-23. American Acad. of Pediatrics, Chicago, Ill. (E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill.)

21. American Soc. of Safety Engineers, annual, Chicago, Ill. (J. B. Johnson, 425 N. Michigan Ave., Chicago 11.)

22-24. Aviation Medicine, 4th annual symp., Santa Monica, Calif. (T. H. Sternberg, UCLA Medical Center, Los Angeles 24, Calif.)

22-26. American Soc. for the Study of Arteriosclerosis, annual, San Francisco, Calif. (O. J. Pollak, P.O. Box 228, Dover, Del.)

23-25. National Soc. of Professional Engineers, San Francisco, Calif. (K. E. Trombley, NSPE, 2029 K St., NE, Washington 6.)

23-25. Rocket Technology and Astronautics, intern., Essen, Germany. (Deutsche Gesellschaft fuer Raketenforschung und Raumfahrt, e.v., Neunsteinerstrasse 19, Stuttgart, Zuffenhausen.)

24-25. International Conference on the Insulin Treatment in Psychiatry, New York, N.Y. (M. Rinkel, 479 Commonwealth Ave., Boston 15, Mass.)

24-25. Taxonomic Consequences of Man's Activities, symp., Mexico, D.F. (H. C. Cutler, Missouri Botanical Garden, St. Louis.)

24-28. American Heart Assoc., San Francisco, Calif. (J. D. Brundage, 44 E. 23 St., New York 10.)

27-28. Plant Physiology, 9th annual research cong., Saskatoon, Saskatchewan, Canada. (D. T. Coupland, Plant Ecology College of Agriculture, Univ. of Saskatchewan, Saskatoon.)

27-29. Radio, Institute of Radio Engineers, fall meeting, Rochester, N.Y. (V. M. Graham, EIA, 11 W. 42 St., N.Y.)

27-31. American Inst. of Electrical Engineers, fall general, Pittsburgh, Pa. (N. S. Hibshman, AIEE, 33 W. 39 St., New York 18.)

27-31. American Public Health Assoc., St. Louis, Mo. (B. F. Mattison, 1790 Broadway, New York 19.)

27-31. Vertebrate Speciation Conf., Univ. of Texas, Austin. (W. F. Blair, Dept. of Zoology, Univ. of Texas, Austin 12.)

27-1. Mental Health, 3rd Latin American cong., Lima, Peru. (B. Caravedo, Comite Peruano Organizador, III Congreso Latinoamericano pro Salud Mental, Avenida del Golf 1040, San Isidro, Lima.)

30-31. Plastics, intern. symp., Philadelphia, Pa. (ASTM, 1916 Race St., Philadelphia 3.)

30-1. American Assoc. of Textile Chemists and Colorists, 37th natl. conv., Chicago, Ill. (J. G. Kelley, E. I. duPont de Nemours & Co., Inc., 7 South Dearborn St., Chicago 3.)

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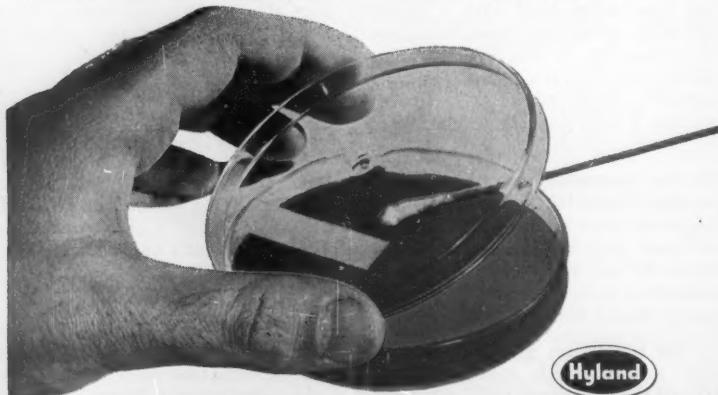
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■ HALOGEN LEAK DETECTOR responds only to increases in the amount of tracer gas present, making it unnecessary to wait for the instrument to clear itself. Four models are available for specific applications including high-speed checking of parts being conveyed past the detector and detection of leaks in vacuum systems operating at 1 to 500  $\mu\text{-Hg}$  or at 20 mm-Hg and above. (General Electric Co., Dept. 225)

■ DIGITAL READOUT presents numbers in a single plane with no overlapping characters. The device employs a simple projection system. Lamp life is said to be from 7000 to 8000 hr. The display consists of four digits and a symbol readout. (Kin Tel, Dept. 242)

■ SCALER of glow-tube type has a capacity of five decimal digits without mechanical registers. Resolving time is 150  $\mu\text{sec}$ . The input sensitivity is 0.25 v negative. A high-voltage supply is variable between 500 and 2500 v. (Baird-Atomic Inc., Dept. 233)

■ FRACTION COLLECTOR for isolating pure gas with chromatograph fractions uses the freeze-out method of collection. The fraction is captured in a U-tube of pure silica sand chilled to liquid-nitrogen temperatures. The unit is operated with a rapid single-stroke plunger, and samples may be collected at 5-sec intervals. (Hamilton Co., Dept. 236)

■ CARD-TO-TAPE CONVERTER is a magnetic-core memory unit that stores up to 80 alpha-numeric characters to accommodate the full contents of a standard card. The memory can be filled in a parallel manner directly from card-sensing brushes and can be read serially a character at a time. Reading time can be 14  $\mu\text{sec}$  per character. Provision is made for code conversion. (Telemeter Magnetics Inc., Dept. 226)

■ DIGITAL VOLTMETER measures d-c voltage from 0.001 to 1000 v with  $\pm 0.1$ -percent accuracy. Readout consists of three digits and a polarity and decimal-point

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indication. The display time can be adjusted from 0.1 sec to infinity. Input impedance is 20,000 ohm/v. (Kin Tel, Dept. 243)

■ CARBON DIOXIDE EQUILIBRATION APPARATUS may be attached directly to a tank of gas. The device includes a needle-needle assembly, glass-bead trap, and a syringe-needle adapter. By means of the apparatus, gas is bubbled through a serum sample, completely saturating a 1.5-ml sample within 3 min. (Will Corporation, Dept. 237)

■ AIR PARTICLE MONITOR indicates detection and measurement of particulate radioactive contamination on a logarithmically calibrated scale covering a range of  $5 \times 10^{-10}$  to  $10^{-6} \mu\text{c}/\text{cm}^3$ . Any preset level can be used to trigger a warning. The equipment is comprised of a computer unit and a pump unit. The computer unit consists of a beta scintillation counter, photomultiplier, and amplifier circuits. (Fairchild Camera and Instrument Corp., Dept. 240)

■ AUDIO SIGNAL GENERATOR operates on the heterodyne principle from 2 to 4000 cy/sec. The frequency scale is logarithmic. A built-in voltmeter provides an output indication that is accurate to  $\pm 2$  percent. Frequency scanning and output regulation are automatic. (Brush Instruments, Dept. 210)

■ VOLTMETER uses suppressed zero to achieve  $\pm \frac{1}{2}$  percent accuracy over a narrow range. Accuracy is maintained without ovens over the temperature range  $-55^\circ$  to  $+65^\circ\text{C}$  and over the frequency range 50 to 2000 cy/sec. Both d-c and a-c types are available. (Voltron Products, Dept. 211)

■ DIGITAL ACTUATOR MOTOR is capable of stepping rates up to 60 per second with travel of 180 deg/step. Used with a 180-to-1 gear ratio, the actuator produces 80 in. oz of torque for a 1-deg step. The weight of the motor and relay box is 1.3 lb. (Digitran Co., Dept. 215)

■ INDUCTANCE METER measures inductance between 0.05  $\mu\text{h}$  and 100 mh. The instrument consists of an oscillator, tunable over the range of 16 kcy/sec to 5 Mcy/sec, loosely coupled to a resonant circuit consisting of a fixed capacitor and the inductance to be measured. The resonance point is indicated by an electron indicator tube. Provision is made for measurement of low capacitance and for approximate value of  $Q$ . (Wayne-Kerr Instruments, Dept. 256)

■ WORLD-TIME CLOCK uses signals picked up from the National Bureau of Standards Station WWV. Compensation is provided for propagation errors. Time

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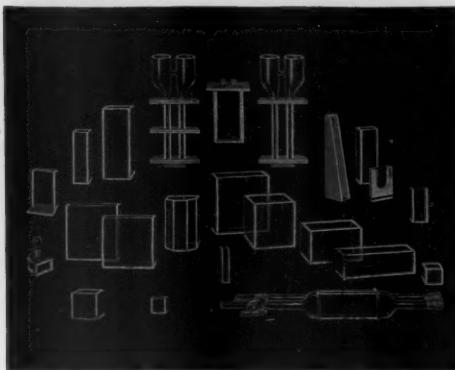
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DIHYDROTHYMIDINE (pfs)	500 mg	50.00
DIHYDROTHYMINYL (pfs) (4,5- (or 5,6)-Dihydro-5-methyl-2,4-dihydropyrimidine)	10 g	10.00
DIHYDRO URACIL (pfs) 5,6-Dihydro-2,4-dihydroxy-pyrimidine	25 g	22.50
DIHYDROURIDINE (Syrup containing approx. 3% H <sub>2</sub> O)	5 g	5.00
DIHYDROXYACETONE (pfs)	25 g	20.00
2,6-DIHYDROXY-4-AMINO-5-NITROSO-PYRIMIDINE	5 mg	7.00
See 4-Amino-2,6-dihydroxy-5-nitrosopyrimidine	500 mg	50.00
2,4-DIHYDROXY-6-METHYL-5-NITRO-PYRIMIDINE	25 g	37.50
(pfs) (5-Nitro-6-methyl uracil)	5 g	10.00
2,4-DIHYDROXY-6-METHYL PYRIMIDINE—See 6-Methyl uracil	25 g	37.50
2,4-DIHYDROXY-5-NITROPYRIMIDINE—See 5-Nitouracil	25 g	37.50
4,6-DIHYDROXY-5-NITROPYRIMIDINE (5-Nitro-4,6-Dihydroxypyrimidine) (pfs)	10 g	27.50
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2,6-DIHYDROXYPURINE—See Xanthine	1 g	75.00
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4,6-DIHYDROXYPYRIMIDINE (pfs)	5 g	7.00
2,4-DIHYDROXYPYRIMIDINE-6-METHYL SULFONE (pfs)	25 g	30.00
2,4-DIHYDROXYPYRIMIDINE-6-SULFONAMIDE (pfs)	100 mg	15.00
See Uracil-6-sulfonamide	1 g	75.00
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See 2-Thiobarbituric acid	100 mg	4.00
3,5-DIOODO-L-TYROSINE (pfs) Sigma Grade	25 g	2.65
4,6-DIMETHYL-2-THIOPYRIMIDINE (pfs)	1 g	3.00
3,5-DINITRO-L-TYROSINE (pfs)	1 g	3.40
2,4-DINITROPHENYLHYDRAZINE (pfs)	10 g	2.00

2,4-DINITRO PHENYL HYDRAZINE SOLN. Stock No. 490-9. For SCO-T per Cabaud, Wroblewski, etc. 100 ml	1.75
2,4-DIPHENYLHYDRAZINE Standard Solution. Stock No. 505-2 For Determination of Transaminase per Bull, 505.	100 ml
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is indicated to the nearest millisecond. To synchronize the time at this precision, a stroboscope is used. The 1-sec interval strobe pulse is brought into coincidence with the second ticks of WWV. (Edgerton, Germeshausen & Grier, Inc., Dept. 257)

**SPECTROPHOTOMETER AND REFLECTANCE ATTACHMENT** uses a diffraction grating as the dispersion device to provide monochromatic radiation. The instrument contains a spherical integrator and a reflectance measuring system designed so that fading, chipping, or stain-

ing of the interior surface of the sphere will not affect accuracy. Very small samples can be measured. A trichromatic chart permits the conversion of reflectance readings to standard C.I.E. trichromatic values. (Bausch and Lomb Optical Co., Dept. 301)

**MOISTURE METER** for gaseous mixtures has six ranges from 0 to 20,000 parts per million; the smallest full-scale range is 0 to 10 parts per million. The instrument operates on the electrolysis principle, whereby the current required to electrolyze all of the water indicates

water content. Sample flow is precisely controlled at temperatures up to 100°C and at pressures of 10 to 40 lb/in.<sup>2</sup> (gage). Output voltage can be adjusted from 10 to 110 mv full scale for input to recorders. (Consolidated Electrodynamics Corp., Dept. 249)

**PREAMPLIFIER** operates with the manufacturer's 12 in. strip-chart potentiometer recorder to provide full-scale deflections in 0.25 sec with input signals of 20  $\mu$ v d-c. The amplifier is a carrier type with differential input, 20-cy/sec frequency response, 1- $\mu$ v noise, and drift and gains as high as 100,000. Full-scale output is 10 mv from a voltage divider, or 10 v without the voltage divider. (Minneapolis-Honeywell, Dept. 251)

**VACUUM-JACKETED TRANSFER LINES** featuring heat transfer as small as 5.5 to 11 Btu/ft hr are available in sections up to 40 ft long and in diameters of 1.25 and 3 in. Lines are treated on the outside to reduce radiative heat transfer, then surrounded with a vacuum jacket that is pumped down to a pressure of  $1 \times 10^{-5}$  mm-Hg or lower. (Consolidated Electrodynamics, Dept. 252)

**COMBINATION VACUUM AND PRESSURE PUMP** consists of a vane-type, dry-air pressure pump and an oil-wetted, rotary-vane-type vacuum pump mounted at opposite ends of an electric motor. The unit will deliver 400 in.<sup>3</sup>/min at 300 lb/in.<sup>2</sup> (gage), and produces a vacuum of 0.20 in.-Hg. (Lear, Inc., Dept. 258)

**PRESSURE TRANSDUCER** combines a Bourdon-tube sensing element and a variable-inductance pick-up. Excitation is normally 30 v at 400 cy/sec. The full-scale output is 0.1 v d-c/v a-c. Ranges from 15 to 3000 lb/in.<sup>2</sup> full scale are available. Response is constant to 10 cy/sec. Hysteresis is 0.5 percent of full scale. Sensitivity is 0.1 percent, repeatability 0.2 percent. (Servomechanisms, Inc., Dept. 255)

**OPTICAL GAGE** measures depth, thickness, height, and diameter over a range of 0 to 3 in. without masters or set gages. Measurements are read on an illuminated, magnified scale graduated in least-reading intervals of 0.0001 in. with accuracy of 25  $\mu$ in. The master scale from which the scale is made is ruled on a diffraction-grating ruling engine. Objects to be measured are laid on an anvil flat to an accuracy of 5  $\mu$ in. A control knob lowers a spindle until it contacts the object being measured. The spindle stops automatically on contact with the object, and the measurement may be read immediately. (Bausch & Lomb Optical Co., Dept. 250)

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National Bureau of Standards

SCIENCE, VOL. 128

# "LAB-ASCO-VAC"

## PORTABLE LABORATORY HIGH-VACUUM PUMP

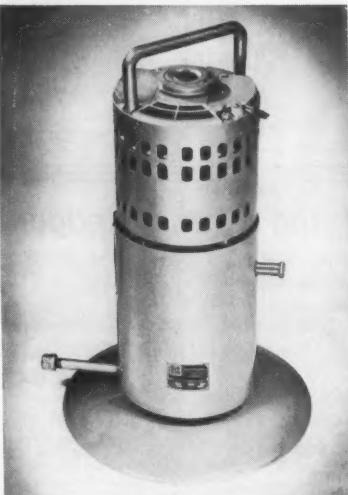
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Noise is eliminated by insulation and rubber mounting, and with vertical design, the conventional belt and pulley have been eliminated. These features, unique to LAB-ASCO-VAC, permit a carrying handle for easy portability.

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The LAB-ASCO-VAC 10 mechanical pump is designed to run cooler. A unique capillary gas ballast cleaner provides efficient operation for longer periods.



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Pumping (displacement) Speed	50 liters/min.
Operating Speed	1140 rpm
Oil Charge Required	1 pint
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Diameter	12 inches
Weight	45 lbs.
Voltage	110/220
Cycles	50/60
Price	\$195.00

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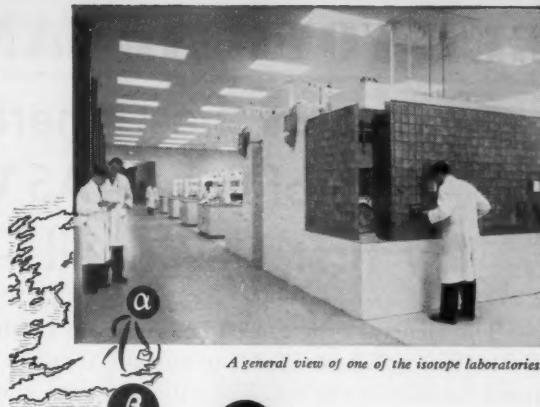
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15 AUGUST 1958

Stern

OL. 128



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2. The six sessions of the Conference on Scientific Communication Problems.
3. Programs of the 18 AAAS sections (symposia and contributed papers).
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5. The Special Sessions: AAAS, Academy Conference, Conference on Scientific Manpower, National Geographic Society, Phi Beta Kappa, Sigma Xi, RESA.
6. Details of the Sheraton-Park Hotel—center of the Meeting—and of the other hotels and session sites.
7. Titles of the latest foreign and domestic scientific films to be shown in the AAAS Science Theatre.
8. Exhibitors in the 1958 Annual Exposition of Science and Industry and descriptions of their exhibits.

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2. Complete roll of AAAS presidents and their fields.
3. The 279 affiliated organizations.
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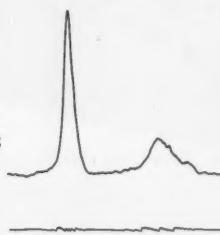
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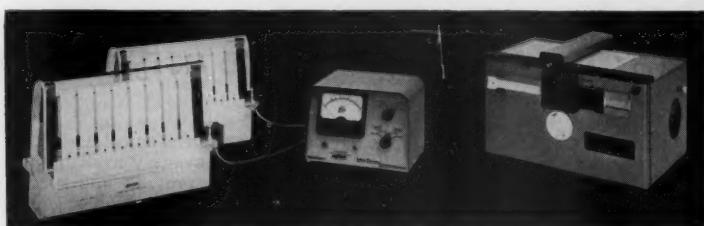
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